STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 123596

TO: Maury Audet **Location: REM/3D20/3D11** **Art Unit: 1654** **Thursday, June 03, 2004** **Case Serial Number: 09/937484**	**From: Barb O'Bryen** **Location: Biotech-Chem Library** **Remsen 1A69** **Phone: 571-272-2518** BOB **barbara.obryen@uspto.gov**

Search Notes

RUSH

Maury,

ECL is also an acronym of for enterochromaffin-like (cells). This lead to false drops. Neither ECL or nor ECA produced useful hits, so they don't appear in the queries I've printed.

Barb

STIC-Biotech/ChemLib 123596

From: Chan, Christina
Sent: Wednesday, June 02, 2004 4:18 PM
To: Audet, Maury; STIC-Biotech/ChemLib
Subject: RE: 09/937484-RUSH Conjugate/Compound Search

Please rush. Thanks Chris

Chris Chan
TC 1600 New Hire Training Coordinator and SPE 1644 & 1642
(571)-272-0841
Remsen, 3E89

-----Original Message-----
From: Audet, Maury
Sent: Wednesday, June 02, 2004 1:23 PM
To: STIC-Biotech/ChemLib; Chan, Christina
Subject: 09/937484-RUSH Conjugate/Compound Search

Greetings,

If possible could I please get a RUSH search (2 month amended) on the following:

Registry/CAPlus, etc. search of (method of use):

TREATMENT of C-FIBRE NEURON ACTIVITY USING:
Compound alone of "Erythrina cristagalli lectin" or ECL or ECA (referred to by all three names/abbrev.)
OR
The same compound within any type of conjugate/composition.

This is the elected invention, no other species (however, if nothing is found, a search for LECTINS generally for treatment of C-fiBRE NEURON activity or ANY NEURON activity could be done; sorry I don't have more - this is a pretty indefinite treatment possibility Applicant's have claimed).

I do not have the structure attached (but hopefully it comes up alright by name in a Registry/STN search of compound), but the lectin is a glycopeptide/protein isolated from such sources as castor beans and coral trees (I believe the latter as well).

I have term searched for some time for the use of this compound in such a method, but have not found a lot, so wanted to follow up with your expertise.

Thanks, Maury

Maury Audet
Patent Examiner A.U. 1654
REM 3D20
Mail Box REM 3D11

Searcher:_____
Phone:_____
Location:_____
Date Picked Up:_____
Date Completed:_____
Searcher Prep/Review:_____
Clerical:_____
Online time:_____

TYPE OF SEARCH:
NA Sequences:_____
AA Sequences:_____
Structures:_____
Bibliographic:_____
Litigation:_____
Full text:_____
Patent Family:_____
Other:_____

VENDOR/COST (where applic.)
STN:_____
DIALOG:_____
Questel/Orbit:_____
DRLink:_____
Lexis/Nexis:_____
Sequence Sys.:_____
WWW/Internet:_____
Other (specify):_____

STIC SEARCH RESULTS FEEDBACK FORM

Biotech-Chem Library

Questions about the scope or the results of the search? Contact ***the searcher or contact***:

Mary Hale, Information Branch Supervisor
Remsen Bldg. 01 D86
571-272-2507

Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* ☐ *Example: 1610*
- *Relevant prior art **found**, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
  (journal articles, conference proceedings, new product announcements etc.)

- *Relevant prior art **not found**:*
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC-Biotech-Chem Library Remsen Bldg.

```
=> fil capl;  d que l6; fil medl; d que l34; fil embase; d que l49
FILE 'CAPLUS' ENTERED AT 12:55:55 ON 03 JUN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 3 Jun 2004  VOL 140 ISS 23
FILE LAST UPDATED: 2 Jun 2004  (20040602/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE


L1          499 SEA FILE=CAPLUS ABB=ON  FOSTER K?/AU
L2           31 SEA FILE=CAPLUS ABB=ON  CHADDOCK J?/AU
L3            9 SEA FILE=CAPLUS ABB=ON  L1 AND L2
L4          351 SEA FILE=CAPLUS ABB=ON  QUINN C?/AU
L5            8 SEA FILE=CAPLUS ABB=ON  L3 AND L4
L6            1 SEA FILE=CAPLUS ABB=ON  FIBER/TI AND L5


FILE 'MEDLINE' ENTERED AT 12:55:55 ON 03 JUN 2004

 FILE LAST UPDATED: 2 JUN 2004 (20040602/UP).  FILE COVERS 1951 TO DATE.

 On February 29, 2004, the 2004 MeSH terms were loaded.  See HELP RLOAD
 for details. OLDMEDLINE now back to 1951.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2004 vocabulary.  See http://www.nlm.nih.gov/mesh/ and
 http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a
 description of changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L23         369 SEA FILE=MEDLINE ABB=ON  FOSTER K?/AU
L24          14 SEA FILE=MEDLINE ABB=ON  CHADDOCK J?/AU
L25         277 SEA FILE=MEDLINE ABB=ON  QUINN C?/AU
L27       34004 SEA FILE=MEDLINE ABB=ON  PLANT LECTINS+NT/CT
L28       61554 SEA FILE=MEDLINE ABB=ON  LECTINS+NT/CT
L29         152 SEA FILE=MEDLINE ABB=ON  ERYTHRINA/CT
L34           2 SEA FILE=MEDLINE ABB=ON  L23 AND L24 AND L25 AND (L27 OR (L28
                AND L29))
```

FILE 'EMBASE' ENTERED AT 12:55:55 ON 03 JUN 2004

FILE COVERS 1974 TO 28 May 2004 (20040528/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
L40          300 SEA FILE=EMBASE ABB=ON  FOSTER K?/AU
L41           11 SEA FILE=EMBASE ABB=ON  CHADDOCK J?/AU
L42          213 SEA FILE=EMBASE ABB=ON  QUINN C?/AU
L44          330 SEA FILE=EMBASE ABB=ON  ERYTHRINA
L49            1 SEA FILE=EMBASE ABB=ON  (L40 OR L41 OR L42) AND L44
```

```
=> dup rem l34,l6,l49
```

FILE 'MEDLINE' ENTERED AT 12:55:56 ON 03 JUN 2004

FILE 'CAPLUS' ENTERED AT 12:55:56 ON 03 JUN 2004

FILE 'EMBASE' ENTERED AT 12:55:56 ON 03 JUN 2004

PROCESSING COMPLETED FOR L34
PROCESSING COMPLETED FOR L6
PROCESSING COMPLETED FOR L49
L82 3 DUP REM L34 L6 L49 (1 DUPLICATE REMOVED)
ANSWERS '1-2' FROM FILE MEDLINE
ANSWER '3' FROM FILE CAPLUS

```
=> d iall 1-2; d ibib ed ab 3
```

L82 ANSWER 1 OF 3 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2002470902 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12105193
TITLE: Inhibition of release of neurotransmitters from rat dorsal root ganglia by a novel conjugate of a Clostridium botulinum toxin A endopeptidase fragment and Erythrina cristagalli lectin.
AUTHOR: Duggan Michael J; **Quinn Conrad P**; **Chaddock John A**; Purkiss John R; Alexander Frances C G; Doward Sarah; Fooks Sarah J; Friis Lorna M; Hall Yper H J; Kirby Elizabeth R; Leeds Nicola; Moulsdale Hilary J; Dickenson Anthony; Green G Mark; Rahman Wahida; Suzuki Rie; Shone Clifford C; **Foster Keith A**
CORPORATE SOURCE: Centre for Applied Microbiology and Research, Porton Down, Salisbury, Wiltshire SP4 0JG, United Kingdom.
SOURCE: Journal of biological chemistry, (2002 Sep 20) 277 (38) 34846-52.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 20020917

Last Updated on STN: 20030105
Entered Medline: 20021024

ABSTRACT:
Clostridial neurotoxins potently and specifically inhibit neurotransmitter release in defined cell types. Here we report that a catalytically active derivative (termed LH(N)/A) of the type A neurotoxin from Clostridium botulinum has been coupled to a lectin obtained from Erythrina cristagalli to form a novel conjugate. This conjugate exhibits an in vitro selectivity for nociceptive afferents compared with the anatomically adjacent spinal neurons, as assessed using in vitro primary neuronal culture systems to measure inhibition of release of neurotransmitters. Chemical conjugates prepared between E. cristagalli lectin and either natively sourced LH(N)/A or recombinant LH(N)/A purified from Escherichia coli are assessed, and equivalence of the recombinant material are demonstrated. Furthermore, the dependence of inhibition of neurotransmitter release on the cleavage of SNAP-25 is demonstrated through the use of an endopeptidase-deficient LH(N)/A conjugate variant. The duration of action of inhibition of neurotransmitter released by the conjugate in vitro is assessed and is comparable with that observed with Clostridium botulinum neurotoxin. Finally, in vivo electrophysiology shows that these in vitro actions have biological relevance in that sensory transmission from nociceptive afferents through the spinal cord is significantly attenuated. These data demonstrate that the potent endopeptidase activity of clostridial neurotoxins can be selectively retargeted to cells of interest and that inhibition of release of neurotransmitters from a neuronal population of therapeutic relevance to the treatment of pain can be achieved.

CONTROLLED TERM: Check Tags: Support, Non-U.S. Gov't
Animals
Base Sequence
Botulinum Toxins: CH, chemistry
*Botulinum Toxins: PD, pharmacology
Cells, Cultured
DNA Primers
Endopeptidases: IP, isolation & purification
*Endopeptidases: PD, pharmacology
*Ganglia, Spinal: DE, drug effects
Ganglia, Spinal: ME, metabolism
*Lectins: PD, pharmacology
*Neurotransmitters: ME, metabolism
Peptide Fragments: IP, isolation & purification
*Peptide Fragments: PD, pharmacology
***Plant Lectins**
Rats
Recombinant Proteins: CH, chemistry
Recombinant Proteins: IP, isolation & purification
Recombinant Proteins: PD, pharmacology

CHEMICAL NAME: 0 (Botulinum Toxins); 0 (DNA Primers); 0 (Lectins); 0 (Neurotransmitters); 0 (Peptide Fragments); 0 (Plant Lectins); 0 (Recombinant Proteins); 0 (erythrina lectin); EC 3.4.- (Endopeptidases)

L82 ANSWER 2 OF 3 MEDLINE on STN
ACCESSION NUMBER: 2000231793 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10768948
TITLE: Inhibition of vesicular secretion in both neuronal and nonneuronal cells by a retargeted endopeptidase derivative of Clostridium botulinum neurotoxin type A.

AUTHOR: **Chaddock J A**; Purkiss J R; Friis L M; Broadbridge J D; Duggan M J; Fooks S J; Shone C C; **Quinn C P**; **Foster K A**
CORPORATE SOURCE: Centre for Applied Microbiology & Research, Porton Down, Salisbury, Wiltshire SP4 0JG, United Kingdom..
john.chaddock@camr.org.uk

OURCE: Infection and immunity, (2000 May) 68 (5) 2587-93.
Journal code: 0246127. ISSN: 0019-9567.
UB. COUNTRY: United States
OCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
ANGUAGE: English
ILE SEGMENT: Priority Journals
NTRY MONTH: 200006
NTRY DATE: Entered STN: 20000622
Last Updated on STN: 20000622
Entered Medline: 20000613

BSTRACT:
lostridial neurotoxins potently and specifically inhibit neurotransmitter elease in defined cell types by a mechanism that involves cleavage of specific omponents of the vesicle docking/fusion complex, the SNARE complex. A erivative of the type A neurotoxin from Clostridium botulinum (termed LH(N)/A) hat retains catalytic activity can be prepared by proteolysis. The LH(N)/A, owever, lacks the putative native binding domain (H(C)) of the neurotoxin and s thus unable to bind to neurons and effect inhibition of neurotransmitter elease. Here we report the chemical conjugation of LH(N)/A to an alternative ell-binding ligand, wheat germ agglutinin (WGA). When applied to a variety of ell lines, including those that are ordinarily resistant to the effects of eurotoxin, WGA-LH(N)/A conjugate potently inhibits secretory responses in hose cells. Inhibition of release is demonstrated to be ligand mediated and ose dependent and to occur via a mechanism involving endopeptidase-dependent leavage of the natural botulinum neurotoxin type A substrate. These data onfirm that the function of the H(C) domain of C. botulinum neurotoxin type A s limited to binding to cell surface moieties. The data also demonstrate that he endopeptidase and translocation functions of the neurotoxin are effective n a range of cell types, including those of nonneuronal origin. These bservations lead to the conclusion that a clostridial endopeptidase conjugate hat can be used to investigate SNARE-mediated processes in a variety of cells as been successfully generated.

ONTROLLED TERM: Animals
*Botulinum Toxin Type A: ME, metabolism
Cell Line
*Clostridium botulinum: ME, metabolism
*Endopeptidases: ME, metabolism
Glycine: ME, metabolism
Insulin: ME, metabolism
*Neurons: ME, metabolism
Neurotransmitters: ME, metabolism
PC12 Cells
Rats
Tritium
Wheat Germ Agglutinins: IP, isolation & purification
Wheat Germ Agglutinins: ME, metabolism
AS REGISTRY NO.: 10028-17-8 (Tritium); 11061-68-0 (Insulin); 56-40-6 (Glycine)
HEMICAL NAME: 0 (Botulinum Toxin Type A); 0 (Neurotransmitters); 0 (Wheat Germ Agglutinins); EC 3.4.- (Endopeptidases)

82 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
CCESSION NUMBER: 2000:706999 CAPLUS
OCUMENT NUMBER: 133:261538
ITLE: Use of a lectin or lectin conjugate for modulation of **C-fiber** activity, and therapeutic use thereof
NVENTOR(S): **Foster, Keith Alan; Chaddock, John**

Searched by Barb O'Bryen, STIC 571-272-2518

ATENT ASSIGNEE(S): **Andrew; Quinn, Conrad Padraig**
Microbiological Research Authority, UK
OURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
OCUMENT TYPE: Patent
ANGUAGE: English
AMILY ACC. NUM. COUNT: 1
ATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000057897	A1	20001005	WO 2000-GB1247	20000331
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1165114	A1	20020102	EP 2000-914295	20000331
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

RIORITY APPLN. INFO.: GB 1999-7429 A 19990331
WO 2000-GB1247 W 20000331

APP

D Entered STN: 06 Oct 2000

B The invention relates to the treatment of pain and to compds. that modulate C-fiber activity. In particular, the invention relates to the use of a lectin in the manuf. of a medicament for modulation of C-fiber neuron activity, and to lectin conjugates. The lectin conjugates comprise a lectin coupled to a peptide or protein, wherein the peptide or protein is substantially free of Clostridial neurotoxin enzyme activity. The invention also concerns methods for manufg. the conjugates. The compds. and compns. described have particular application in the treatment of diseases of which C-fiber activity is a component. Such diseases include pain, inflammation, psoriasis and other C-fiber related conditions.

EFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> fil capl; d que l15; d que l19; d que l22
FILE 'CAPLUS' ENTERED AT 12:58:06 ON 03 JUN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 3 Jun 2004  VOL 140 ISS 23
FILE LAST UPDATED: 2 Jun 2004  (20040602/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE


L10          705 SEA FILE=CAPLUS ABB=ON  NERVE/CT(L)(C/OBI(W)(FIBER#/OBI OR
                 FIBRE#/OBI))
L11          900 SEA FILE=CAPLUS ABB=ON  ERYTHRINA/OBI
L12        24970 SEA FILE=CAPLUS ABB=ON  LECTIN#/OBI
L14          487 SEA FILE=CAPLUS ABB=ON  ECL/OBI OR ECA/OBI
L15            1 SEA FILE=CAPLUS ABB=ON  L10 AND (L14 OR (L11 AND L12))



L11          900 SEA FILE=CAPLUS ABB=ON  ERYTHRINA/OBI
L12        24970 SEA FILE=CAPLUS ABB=ON  LECTIN#/OBI
L16        97353 SEA FILE=CAPLUS ABB=ON  NEURON?/OBI
L17       143736 SEA FILE=CAPLUS ABB=ON  NERVE/CT
L19            3 SEA FILE=CAPLUS ABB=ON  ((L16 OR L17)) AND ((L11 AND L12))



L10          705 SEA FILE=CAPLUS ABB=ON  NERVE/CT(L)(C/OBI(W)(FIBER#/OBI OR
                 FIBRE#/OBI))
L12        24970 SEA FILE=CAPLUS ABB=ON  LECTIN#/OBI
L22            6 SEA FILE=CAPLUS ABB=ON  L10 AND L12 AND (MUCUS/OBI OR PAIN/OBI)


=> s (l15 or l19 or l22) not l6

L83            7 (L15 OR L19 OR L22) NOT (L6)
```

previously searched w/ inventor search

```
=> fil medl; d que l38; d que l39

FILE 'MEDLINE' ENTERED AT 12:58:07 ON 03 JUN 2004

 FILE LAST UPDATED: 2 JUN 2004 (20040602/UP).  FILE COVERS 1951 TO DATE.

 On February 29, 2004, the 2004 MeSH terms were loaded.  See HELP RLOAD
```

for details. OLDMEDLINE now back to 1951.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a description of changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
L29          152 SEA FILE=MEDLINE ABB=ON  ERYTHRINA/CT
L30        71561 SEA FILE=MEDLINE ABB=ON  NERVE FIBERS+NT/CT
L38            0 SEA FILE=MEDLINE ABB=ON  L29 AND L30
```

```
L7          1861 SEA FILE=MEDLINE ABB=ON  C FIBER#
L28        61554 SEA FILE=MEDLINE ABB=ON  LECTINS+NT/CT
L29          152 SEA FILE=MEDLINE ABB=ON  ERYTHRINA/CT
L30        71561 SEA FILE=MEDLINE ABB=ON  NERVE FIBERS+NT/CT
L31          956 SEA FILE=MEDLINE ABB=ON  L7 AND L30
L36         5223 SEA FILE=MEDLINE ABB=ON  PLANT LECTINS/CT
L39            2 SEA FILE=MEDLINE ABB=ON  (L36 OR (L28 AND L29)) AND L31
```

```
=> s l39 not l34
L84            2 L39 NOT L34
```

```
=> fil embase;d que l51

FILE 'EMBASE' ENTERED AT 12:58:08 ON 03 JUN 2004
COPYRIGHT (C) 2004 Elsevier Inc. All rights reserved.

 FILE COVERS 1974 TO 28 May 2004 (20040528/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.
```

```
L44          330 SEA FILE=EMBASE ABB=ON  ERYTHRINA
L46         1169 SEA FILE=EMBASE ABB=ON  NERVE FIBER C/CT
L51            0 SEA FILE=EMBASE ABB=ON  L44 AND L46
```

```
=> fil napra;d que l60

FILE 'NAPRALERT' ENTERED AT 12:58:09 ON 03 JUN 2004
COPYRIGHT (C) 2004 Board of Trustees of the University of Illinois,
University of Illinois at Chicago.

    ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~

    Some records in this file are extremely long when displayed in
    the ALL format. The CHC (Character Count) field can be used to
    estimate record length. Type HELP CONTENT at the next arrow
    prompt (=>) for data content and search strategy information.

    ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
```

FILE COVERS 1650 TO 11 MAY 2004 (20040511/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

L55 397 SEA FILE=NAPRALERT ABB=ON ERYTHRINA
L56 929 SEA FILE=NAPRALERT ABB=ON NEURON? OR NERVE#
L60 0 SEA FILE=NAPRALERT ABB=ON L55(S)L56

=> fil CANCERLIT, DRUGU, PASCAL, JICST-EPLUS, BIOTECHNO, ESBIOBASE, CABA, LIFESCI,
BIOSIS, TOXCENTER, WPIDS, SCISEARCH

FILE 'CANCERLIT' ENTERED AT 12:58:10 ON 03 JUN 2004

FILE 'DRUGU' ENTERED AT 12:58:10 ON 03 JUN 2004
COPYRIGHT (C) 2004 THOMSON DERWENT

FILE 'PASCAL' ENTERED AT 12:58:10 ON 03 JUN 2004
Any reproduction or dissemination in part or in full,
by means of any process and on any support whatsoever
is prohibited without the prior written agreement of INIST-CNRS.
COPYRIGHT (C) 2004 INIST-CNRS. All rights reserved.

FILE 'JICST-EPLUS' ENTERED AT 12:58:10 ON 03 JUN 2004
COPYRIGHT (C) 2004 Japan Science and Technology Agency (JST)

FILE 'BIOTECHNO' ENTERED AT 12:58:10 ON 03 JUN 2004
COPYRIGHT (C) 2004 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'ESBIOBASE' ENTERED AT 12:58:10 ON 03 JUN 2004
COPYRIGHT (C) 2004 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'CABA' ENTERED AT 12:58:10 ON 03 JUN 2004
COPYRIGHT (C) 2004 CAB INTERNATIONAL (CABI)

FILE 'LIFESCI' ENTERED AT 12:58:10 ON 03 JUN 2004
COPYRIGHT (C) 2004 Cambridge Scientific Abstracts (CSA)

FILE 'BIOSIS' ENTERED AT 12:58:10 ON 03 JUN 2004
COPYRIGHT (C) 2004 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'TOXCENTER' ENTERED AT 12:58:10 ON 03 JUN 2004
COPYRIGHT (C) 2004 ACS

FILE 'WPIDS' ENTERED AT 12:58:10 ON 03 JUN 2004
COPYRIGHT (C) 2004 THOMSON DERWENT

FILE 'SCISEARCH' ENTERED AT 12:58:10 ON 03 JUN 2004
COPYRIGHT 2004 THOMSON ISI

=> d que l72; d que l75

L66 4582 SEA ERYTHRINA OR CRISTAGALLI OR CRISTA GALLI
L67 134434 SEA LECTIN#
L70 2355985 SEA NEURON? OR NERVE?
L72 33 SEA L66 AND L67 AND L70

```
L66         4582 SEA ERYTHRINA OR CRISTAGALLI OR CRISTA GALLI
L70      2355985 SEA NEURON? OR NERVE?
L71        45291 SEA C(5A)(FIBER# OR FIBRE#)
L75            2 SEA L66 AND L70 AND L71


=> s l72 or l75

L85           33 L72 OR L75

=> fil uspatf; d que l81

FILE 'USPATFULL' ENTERED AT 12:58:19 ON 03 JUN 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 3 Jun 2004 (20040603/PD)
FILE LAST UPDATED: 3 Jun 2004 (20040603/ED)
HIGHEST GRANTED PATENT NUMBER: US6745393
HIGHEST APPLICATION PUBLICATION NUMBER: US2004107471
CA INDEXING IS CURRENT THROUGH 3 Jun 2004 (20040603/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 3 Jun 2004 (20040603/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Apr 2004
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Apr 2004

>>>  USPAT2 is now available.  USPATFULL contains full text of the     <<<
>>>  original, i.e., the earliest published granted patents or         <<<
>>>  applications.  USPAT2 contains full text of the latest US         <<<
>>>  publications, starting in 2001, for the inventions covered in     <<<
>>>  USPATFULL.  A USPATFULL record contains not only the original     <<<
>>>  published document but also a list of any subsequent              <<<
>>>  publications.  The publication number, patent kind code, and      <<<
>>>  publication date for all the US publications for an invention     <<<
>>>  are displayed in the PI (Patent Information) field of USPATFULL   <<<
>>>  records and may be searched in standard search fields, e.g., /PN, <<<
>>>  /PK, etc.                                                         <<<

>>>  USPATFULL and USPAT2 can be accessed and searched together        <<<
>>>  through the new cluster USPATALL.  Type FILE USPATALL to          <<<
>>>  enter this cluster.                                               <<<
>>>                                                                    <<<
>>>  Use USPATALL when searching terms such as patent assignees,       <<<
>>>  classifications, or claims, that may potentially change from      <<<
>>>  the earliest to the latest publication.                           <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.


L78        12209 SEA FILE=USPATFULL ABB=ON  (NERVE# OR NEURON?)/IT,TI,AB,CLM
L81            1 SEA FILE=USPATFULL ABB=ON  ERYTHRINA AND L78


=> dup rem l84,l83,l85,l81
FILE 'MEDLINE' ENTERED AT 12:58:56 ON 03 JUN 2004

FILE 'CAPLUS' ENTERED AT 12:58:56 ON 03 JUN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'DRUGU' ENTERED AT 12:58:56 ON 03 JUN 2004
```

FILE 'PASCAL' ENTERED AT 12:58:56 ON 03 JUN 2004

FILE 'BIOTECHNO' ENTERED AT 12:58:56 ON 03 JUN 2004

FILE 'ESBIOBASE' ENTERED AT 12:58:56 ON 03 JUN 2004

FILE 'LIFESCI' ENTERED AT 12:58:56 ON 03 JUN 2004

FILE 'BIOSIS' ENTERED AT 12:58:56 ON 03 JUN 2004

FILE 'TOXCENTER' ENTERED AT 12:58:56 ON 03 JUN 2004

FILE 'WPIDS' ENTERED AT 12:58:56 ON 03 JUN 2004

FILE 'SCISEARCH' ENTERED AT 12:58:56 ON 03 JUN 2004

FILE 'USPATFULL' ENTERED AT 12:58:56 ON 03 JUN 2004

PROCESSING COMPLETED FOR L84
PROCESSING COMPLETED FOR L83
PROCESSING COMPLETED FOR L85
PROCESSING COMPLETED FOR L81
L86 26 DUP REM L84 L83 L85 L81 (17 DUPLICATES REMOVED)
ANSWERS '1-2' FROM FILE MEDLINE
ANSWERS '3-9' FROM FILE CAPLUS
ANSWERS '10-12' FROM FILE DRUGU
ANSWERS '13-14' FROM FILE PASCAL
ANSWER '15' FROM FILE ESBIOBASE
ANSWERS '16-21' FROM FILE BIOSIS
ANSWER '22' FROM FILE TOXCENTER
ANSWER '23' FROM FILE WPIDS
ANSWERS '24-25' FROM FILE SCISEARCH
ANSWER '26' FROM FILE USPATFULL

=> d iall 1-25; d ibib ab hit 26; fil hom

L86 ANSWER 1 OF 26 MEDLINE on STN
ACCESSION NUMBER: 2001130385 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11113318
TITLE: Localization of N-methyl-D-aspartate NR2B subunits on primary sensory neurons that give rise to small-caliber sciatic nerve fibers in rats.
AUTHOR: Ma Q P; Hargreaves R J
CORPORATE SOURCE: Department of Pharmacology, Merck Sharp & Dohme Research Laboratories, Neuroscience Research Centre, Terlings Park, CM20 2QR, Harlow, UK.. qingping_ma@merck.com
SOURCE: Neuroscience, (2000) 101 (3) 699-707.
Journal code: 7605074. ISSN: 0306-4522.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010301

ABSTRACT:
In the present study we have used immunohistochemical staining and retrograde tracing techniques to investigate the relationship between the N-methyl-D-aspartate receptor NR2B subunits and small-diameter primary afferent dorsal root ganglion neurons that give rise to the sciatic nerve fibers. Three days after an intra-sciatic nerve injection of tetramethyl rhodamine isothiocyanate-conjugated wheat germ agglutinin which labels small-diameter primary afferents, many NR2B and wheat germ agglutinin-double-labeled cells (approximately 70% of wheat germ agglutinin-labeled neurons) were observed in the L5 dorsal root ganglia. Three days after an intra-sciatic nerve injection of fluorescein isothiocyanate-conjugated Bandeiraea simplicifolia agglutinin isolectin B4 which labels predominantly non-peptidergic **C-fiber*** primary afferents, NR2B and Bandeiraea simplicifolia agglutinin isolectin B4 double-labeled neurons (approximately 90% of Bandeiraea simplicifolia agglutinin isolectin B4-labeled neurons) were also observed in the L5 dorsal root ganglion. Three days after an intra-sciatic nerve injection of fluorescein isothiocyanate-conjugated cholera toxin B subunit, only approximately 40% of cholera toxin B subunit-labeled neurons were NR2B positive and those labeled neurons tended to be small-sized. When calcitonin gene-related peptide and NR2B were labeled by a double immunofluorescent staining technique, we found that the majority of calcitonin gene-related peptide-positive neurons was NR2B immunoreactive (>90% of calcitonin gene-related peptide-positive neurons, and approximately 60% of NR2B-positive neurons) as well. Size frequency analysis also demonstrated that NR2B subunits were predominantly localized on the small and medium-sized neurons.These results suggest that NR2B subunits are predominantly expressed on small diameter primary afferents, and these NR2B containing N-methyl-D-aspartate receptors may play a role in the modulation of neurotransmitter release from primary afferent terminals.

CONTROLLED TERM: Animals
Calcitonin Gene-Related Peptide: ME, metabolism
Cell Count
Cell Size: PH, physiology
Cholera Toxin: PD, pharmacology
Fluorescein-5-isothiocyanate: DU, diagnostic use
Lectins: DU, diagnostic use
***Nerve Fibers: ME, metabolism**
Nerve Fibers: UL, ultrastructure
*Neurons, Afferent: ME, metabolism
Neurons, Afferent: UL, ultrastructure
Nociceptors: ME, metabolism
Nociceptors: UL, ultrastructure
*Pain: ME, metabolism
***Plant Lectins**
Rats
Rats, Sprague-Dawley
*Receptors, N-Methyl-D-Aspartate: ME, metabolism
*Sciatic Nerve: ME, metabolism
Sciatic Nerve: UL, ultrastructure
Wheat Germ Agglutinins: DU, diagnostic use
CAS REGISTRY NO.: 3326-32-7 (Fluorescein-5-isothiocyanate); 83652-28-2 (Calcitonin Gene-Related Peptide); 9012-63-9 (Cholera Toxin)
CHEMICAL NAME: 0 (Griffonia simplicifolia lectins); 0 (Lectins); 0 (NR2B

NMDA receptor); 0 (Plant Lectins); 0 (Receptors, N-Methyl-D-Aspartate); 0 (Wheat Germ Agglutinins)

L86 ANSWER 2 OF 26 MEDLINE on STN
ACCESSION NUMBER: 94110395 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8282849
TITLE: Structure, vascularization, and innervation of the mystacial pad of the rat as revealed by the lectin Griffonia simplicifolia.
AUTHOR: Rice F L
CORPORATE SOURCE: Department of Anatomy, Cell Biology and Neurobiology, Albany Medical College, New York 12208.
SOURCE: Journal of comparative neurology, (1993 Nov 15) 337 (3) 386-99.
Journal code: 0406041. ISSN: 0021-9967.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199402
ENTRY DATE: Entered STN: 19940228
Last Updated on STN: 19940228
Entered Medline: 19940217

ABSTRACT:
The mystacial pad of the rat is endowed with rows of vibrissal follicle-sinus complexes (F-SCs) that receive a dense and rich variety of innervation, much of which is **C fibers**. Each F-SC consists of a follicle at the core of a spindle-shaped, encapsulated vascular sinus. Previous studies have shown that the B subunit of the lectin Griffonia simplicifolia (GSA I-B4) binds selectively to a subset of small neurons in the trigeminal ganglion and to a subset of **C fibers** preferentially distributed to inner lamina II and outer lamina III of nucleus caudalis in the brainstem trigeminal complex in the rat. These laminae are also a major site of termination for afferents in superficial vibrissal nerves (SVNs) that innervate the upper portion of F-SCs. To determine the peripheral distribution of the afferents that bind GSA I-B4, mystacial pads from rats were prepared for fluorescence microscopy with GSA I-B4 conjugated to rhodamine. At the neck of each F-SC, numerous circumferentially oriented bundles of fine-caliber axonal profiles were labeled in the inner conical body, which receives nearly all of its innervation from the SVNs. A sparse, random distribution of fine-caliber profiles from deep vibrissal nerves was labeled at the level of the cavernous sinus in the deep half of the F-SCs. GSA I-B4 also labeled a variety of nonneural structures. By binding to vascular linings, GSA I-B4 revealed a dense, highly organized capillary system within the mesenchymal sheath that forms the inner lining of the vascular sinuses. Thus each F-SC appears to have a closed capillary system within the open vascular sinus. Trabeculae within the lumen of the cavernous sinus were also revealed to span between the sinus capsule and the mesenchymal sheath only about midway along the length of the follicle instead of the entire deeper half, as was previously believed. in addition, GSA I-B4 bound to the surface of follicular cells preferentially in the superficial half of the F-SCs. Sweat glands within the intervibrissal fur and some cells within sebaceous glands in F-SCs were also labeled as well as their ducts. The potential functional implications of these various features are discussed.

CONTROLLED TERM: Check Tags: Male; Support, Non-U.S. Gov't
Animals
Axons: ME, metabolism
Histocytochemistry
Lectins
Microcirculation: PH, physiology
Neurons, Afferent: PH, physiology
***Plant Lectins**

Presynaptic Terminals: ME, metabolism
Rats
Rats, Sprague-Dawley
Sebaceous Glands: CY, cytology
Sebaceous Glands: IR, innervation
Sweat Glands: CY, cytology
Sweat Glands: IR, innervation
Trigeminal Ganglion: CY, cytology
*Vibrissae: AH, anatomy & histology

CHEMICAL NAME: 0 (Griffonia simplicifolia lectins); 0 (Lectins); 0 (Plant Lectins)

L86 ANSWER 3 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 1999:249106 CAPLUS
DOCUMENT NUMBER: 130:276767
ENTRY DATE: Entered STN: 23 Apr 1999
TITLE: Conjugates of galactose-binding lectins and clostridial neurotoxins as analgesics
INVENTOR(S): Duggan, Michael John; Chaddock, John Andrew
PATENT ASSIGNEE(S): The Speywood Laboratory Limited, UK; Microbiological Research Authority
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K047-48
CLASSIFICATION: 1-11 (Pharmacology)
Section cross-reference(s): 63
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

3/31/99 10/7/98

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9917806	A1	19990415	WO 1998-GB3001	19981007
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2306350	AA	19990415	CA 1998-2306350	19981007
AU 9893574	A1	19990427	AU 1998-93574	19981007
AU 741456	B2	20011129		
ZA 9809138	A	19990527	ZA 1998-9138	19981007
EP 996468	A1	20000503	EP 1998-946571	19981007
EP 996468	B1	20030521		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001518522	T2	20011016	JP 2000-514674	19981007
AT 240747	E	20030615	AT 1998-946571	19981007
PT 996468	T	20030930	PT 1998-946571	19981007

PRIORITY APPLN. INFO.: GB 1997-21189 A 19971008
WO 1998-GB3001 W 19981007

ABSTRACT:
A class of novel agents that are able to modify nociceptive afferent function is provided. The agents may inhibit the release of neurotransmitters from discrete populations of neurons and thereby reduce or preferably prevent the transmission of afferent pain signals from peripheral to central pain fibers. They comprise a galactose-binding lectin linked to a deriv. of a clostridial

eurotoxin. The deriv. of the clostridial neurotoxin comprises the L-chain, or fragment thereof, which includes the active proteolytic enzyme domain of the ight (L) chain, linked to a mol. or domain with membrane-translocating ctivity. The agents may be used in or as pharmaceuticals for the treatment of ain, particularly chronic pain.

UPPL. TERM: analgesic neurotoxin conjugate galactose binding **lectin**

NDEX TERM: Analgesics
Molecular cloning
(conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

NDEX TERM: Agglutinins and **Lectins**
ROLE: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(galactose-binding, conjugates with clostridial neurotoxins; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

NDEX TERM: Bandeiraea simplicifolia
Erythrina
Erythrina corallodendron
Erythrina crista-galli
Peanut (Arachis hypogaea)
Pseudomonas aeruginosa
Soybean (Glycine max)
(**lectins** of; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

NDEX TERM: **Nerve**
(motor, binding to; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

NDEX TERM: Neurohormones
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(neuromodulators, release of; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

NDEX TERM: Transport proteins
ROLE: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(neurotoxin domain contg.; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

NDEX TERM: Clostridium
Clostridium botulinum
Clostridium tetani
(neurotoxin of; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

NDEX TERM: Toxins
ROLE: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(neurotoxins, of Clostridium; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

DEX TERM: Neurotransmitters
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(release of; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

DEX TERM: **Nerve**
(sensory, nociceptive; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

DEX TERM: Oligosaccharides, biological studies
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.alpha.- and .beta.-D-galactosyl; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

DEX TERM: 1811-31-0, N-Acetylgalactosamine
ROLE: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

DEX TERM: 107231-12-9, Botulin
ROLE: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

DEX TERM: 59-23-4, Galactose, biological studies
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**lectins** binding; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

DEX TERM: 9001-92-7, Proteinase
ROLE: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(neurotoxin domain contg.; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

DEX TERM: 56-40-6, Glycine, biological studies 56-86-0, Glutamic acid, biological studies 33507-63-0, Substance p
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(release of; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

FERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD.

FERENCE(S):
(1) Allergan Inc; WO 9428923 A 1994 CAPLUS
(2) Dolly, J; WO 9532738 A 1995 CAPLUS
(3) Foster, K; WO 9633273 A 1996 CAPLUS
(4) Foster, K; WO 9807864 A 1998 CAPLUS
(5) Pascual, D; WO 9718790 A 1997 CAPLUS
(6) Streit; J Histochem Cytochem 1985, V33(10), P1042 CAPLUS

6 ANSWER 4 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 9
CESSION NUMBER: 1988:184082 CAPLUS
CUMENT NUMBER: 108:184082
TRY DATE: Entered STN: 28 May 1988
TLE: Occurrence and distribution of glycoconjugates in human tissues as detected by the **Erythrina**

cristagalli **lectin**

THOR(S): Vierbuchen, Mathias; Uhlenbruck, Gerhard; Ortmann, Monika; Dufhues, Gabriele; Fischer, Robert
RPORATE SOURCE: Inst. Pathol., Univ. Cologne, Cologne, D-5000, Fed. Rep. Ger.

URCE: Journal of Histochemistry and Cytochemistry (1988), 36(4), 367-76
CODEN: JHCYAS; ISSN: 0022-1554
CUMENT TYPE: Journal
ANGUAGE: English
LASSIFICATION: 13-1 (Mammalian Biochemistry)
Section cross-reference(s): 9

STRACT:
rseradish peroxidase-E. cristagalli agglutinin (HRP-ECA) conjugate was used or histochem. staining of tissue sections from various formalin-fixed, araffin-embedded human tissue specimens. The HRP-ECA conjugate showed broad activity, but there was a distinct distribution of native (not masked by alic acid) and sialic acid-masked ECA binding sites in the various organs. ree ECA binding sites could be detected on red blood cells; lymphocytes of the ymus, tonsil, and lymph node; and in mucous substances of different organs. ndependent of blood group type, the vascular endothelium exhibited strong ECA eactivity. Free ECA binding sites occurred in the cytoplasm of Kupffer's ells in liver; in histiocytic cells of thymus, lymph node, and tonsil; and in one marrow. Podocytes of kidney glomerulus, syncytiotrophoblasts of placenta, egakaryocytes in bone marrow, myelin sheath of nerve, medullary thymocytes, nd hepatocytes, as well as pancreatic islet cells, contained only sialic cid-capped ECA binding sites. Inhibition studies with galactose, lactose, and acetyllactosamine, as well as other sugars, revealed that this lectin is pecific for galactosyl residues. ON comparison to galactose and lactose, acetyllactosamine exhibited the highest inhibitory activity on lectin nding, supporting the concept that this lectin is most reactive with acetyllactosamine-type (type 2 chain)glycoconjugates.

UPPL. TERM: acetyllactosamine glycoconjugate organ distribution; **Erythrina lectin** glycoconjugate organ staining

NDEX TERM: Organ
(acetyllactosamine-contg. glycoconjugates distribution in, of human)

NDEX TERM: Sialic acids
ROLE: BIOL (Biological study)
(acetyllactosamine-contg. glycoconjugates masking by, in human tissues)

NDEX TERM: Lymphocyte
(acetyllactosamine-contg. glycoconjugates of, in human tissues)

NDEX TERM: Adrenal cortex, composition
Blood vessel, composition
Bone marrow, composition
Bronchi
Digestive tract
Epididymis
Erythrocyte
Histiocyte
Kidney, composition
Lymph gland
Mammary gland
Muscle, composition
Nerve, composition
Ovary, composition
Oviduct
Pancreas, composition

Placenta
Prostate gland
Stomach, composition
Testis, composition
Thymus gland
Thyroid gland, composition
Tonsil
Uterus, composition
(acetyllactosamine-contg. glycoconjugates of, of human)

INDEX TERM: **Erythrina** crista-galli
(**lectin** of, glycoconjugates of human organs staining by and specificity of)

INDEX TERM: Agglutinins and **Lectins**
ROLE: BIOL (Biological study)
(of **Erythrina** cristagalli, acetyllactosamine glycoconjugates staining by, in human organs)

INDEX TERM: Megakaryocyte
Pancreatic islet of Langerhans
(sialic acid-capped acetyllactosamine-contg. glycoconjugates of, of human)

INDEX TERM: Staining, biological
(with **lectin** of **Erythrina** cristagalli, in human organs)

INDEX TERM: Liver, composition
(Kupffer cell, acetyllactosamine-contg. glycoconjugates of, of human)

INDEX TERM: Bladder
(epithelium, acetyllactosamine-contg. glycoconjugates of, of human)

INDEX TERM: Ureter
(epithelium, acetyllactosamine-contg. glycoconjugates, of human)

INDEX TERM: Reproductive tract
(female, acetyllactosamine-contg. glycoconjugates of, of human)

INDEX TERM: Liver, composition
(hepatocyte, sialic acid-capped acetyllactosamine-contg. glycoconjugates of, of human)

INDEX TERM: Reproductive tract
(male, acetyllactosamine-contg. glycoconjugates of, of human)

INDEX TERM: Salivary gland
(submandibular, acetyllactosamine-contg. glycoconjugates of, of human)

INDEX TERM: Trophoblast
(syncytio-, sialic acid-capped acetyllactosamine-contg. glycoconjugates of, of human)

INDEX TERM: Thymus gland
(thymocyte, sialic acid-capped acetyllactosamine-contg. glycoconjugates of, of human)

INDEX TERM: 59-23-4, D-Galactose, biological studies 63-42-3, Lactose
ROLE: BIOL (Biological study)
(**lectin** of **Erythrina** cristagalli specificity for)

INDEX TERM: 32181-59-2D, N-Acetyllactosamine, glycoconjugates contg.
ROLE: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(of organs, of human, occurrence and distribution of)

L86 ANSWER 5 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:312287 CAPLUS
DOCUMENT NUMBER: 140:315072

ENTRY DATE: Entered STN: 16 Apr 2004
TITLE: Methods and compounds for the treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compounds having targeting and translocating modified light chain of clostridial neurotoxin
INVENTOR(S): Quinn, Conrad Padraig; Foster, Keith Alan; Chaddock, John
PATENT ASSIGNEE(S): Health Protection Agency, USA
SOURCE: U.S. Pat. Appl. Publ., 19 pp., Cont.-in-part of U.S. 6,632,440.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K039-08
US PATENT CLASSIF.: 424239100; 514012000
CLASSIFICATION: 1-9 (Pharmacology)
Section cross-reference(s): 63
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004071736	A1	20040415	US 2003-633698	20030805
WO 2000010598	A2	20000302	WO 1999-GB2806	19990825
WO 2000010598	A3	20000615		
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6632440	B1	20031014	US 2001-763669	20010529

PRIORITY APPLN. INFO.: GB 1998-18548 A 19980825
WO 1999-GB2806 W 19990825
US 2001-763669 A2 20010529

ABSTRACT:
A method of treating mucus hypersecretion, the causative factor in chronic obstructive pulmonary disease (COPD), asthma and other clin. conditions involving COPD, comprises administering a compd. that inhibits exocytosis in mucus secreting cells or neurons that control or direct mucus secretion. Also described is a compd., for use in the treatment of hypersecretion of mucus, which inhibits mucus secretion by inhibiting mucus secretion by mucus secreting cells, and/or inhibiting neurotransmitter release from neuronal cells controlling or directing mucus secretion. The compd. comprises: (a) a light chain (L-chain) or L-chain fragment of a clostridial neurotoxin, which L-chain or L-chain fragment includes the active proteolytic enzyme domain of the L-chain; (b) a targeting domain that binds to a target cell selected from the group consisting of (i) a mucus secreting cell, and (ii) a neuronal cell controlling or directing mucus secretion; and (c) a translocating domain that translocates the L-chain or L-chain fragment into the target cell; with the proviso that the compd. is not a botulinum toxin. Substance P, as the targeting domain, was conjugated to clostridial neurotoxin fragment LHN/A.

SUPPL. TERM: **mucus** hypersecretion treatment clostridial neurotoxin light chain construct; targeting translocating clostridial neurotoxin proteolytic construct; chronic obstructive pulmonary disease treatment; antiasthmatic **mucus** secretion inhibitor; substance P conjugate clostridial neurotoxin light chain
INDEX TERM: **Nerve**
(**C-fiber**, targeting cells of;
treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting

and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Lung
(Clara cell, targeting; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Proteins
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(F, translocating domain of, of SER virus; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Glycoproteins
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(G, translocating domain of, of vesicular stomatitis virus; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Drug delivery systems
(aerosols; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Lung, disease
(chronic obstructive, treatment of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Toxins
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(construct contg. translocating domain of bacterial; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Eubacteria
Microorganism
Virus
(construct contg. translocating domain of protein of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Toxins
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diphtheria, translocating domain of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Toxins
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(exotoxin A, translocating domain of domain II of pseudomonas; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Proteins
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fusogenic, translocating domain of, of Semliki Forest virus; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Neurotransmitters
ROLE: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition of release of, by neurons controlling **mucus** secretion; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Exocytosis
Secretion (process)
(inhibition of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Biological transport
(intracellular, construct with domain for; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Fusion proteins (chimeric proteins)
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(membrane, translocating domain of virally-expressed; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Proteins
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microbial, construct contg. translocating domain of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Drug delivery systems
(nasal; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Nerve

(neuron, controlling **mucus** secretion, inhibition of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Nerve
(nonadrenergic-noncholinergic, targeting cells of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Clostridium botulinum
(not toxin of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Drug delivery systems
(oral; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Animal cell
(secreting **mucus**, inhibition of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Gland
(submucosal, targeting **mucus**-secreting cells of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Protein motifs
(targeting and translocating domains; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Epithelium
(targeting goblet cell of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Cell
(targeting serous; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Toxins
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tetanus, construct contg. light chain of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: SER virus
(translocating domain of F protein of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and

translocating modified light chain of clostridial neurotoxin)

NDEX TERM: Pseudomonas
(translocating domain of domain II of exotoxin A of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

NDEX TERM: Spumavirus
(translocating domain of envelope glycoprotein of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

NDEX TERM: Envelope proteins
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(translocating domain of foamy virus; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

NDEX TERM: Semliki Forest virus
(translocating domain of fusogenic protein of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

NDEX TERM: Vesicular stomatitis virus
(translocating domain of glycoprotein G of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

NDEX TERM: Influenza virus
(translocating domain of hemagglutinin of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

NDEX TERM: Hemagglutinins
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(translocating domain of influenza virus; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

NDEX TERM: Antiasthmatics
Drug delivery systems
Human
Mucus
(treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

NDEX TERM: Asthma
(treatment of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified

light chain of clostridial neurotoxin)

INDEX TERM: Agglutinins and **Lectins**
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(wheat germ, conjugates with LHN/A; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Adrenoceptor agonists
(.beta.2-, targeting domain of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: 9001-92-7, Proteolytic enzyme
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protease, domain of clostridial neurotoxin light chain; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: 33507-63-0, Substance P (peptide) 37221-79-7, Vasoactive intestinal polypeptide 80043-53-4, Gastrin-releasing peptide 83652-28-2, Calcitonin gene-related peptide
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(targeting domain of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: 33507-63-0DP, Substance P (peptide), conjugates with LHN/A
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: 679058-76-5
ROLE: PRP (Properties)
(unclaimed protein sequence; methods and compds. for the treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: 54017-28-6 91859-00-6 117138-19-9 158734-08-8 259653-92-4 259653-93-5 302566-59-2
ROLE: PRP (Properties)
(unclaimed sequence; methods and compds. for the treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

L86 ANSWER 6 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:991382 CAPLUS
DOCUMENT NUMBER: 140:31455
ENTRY DATE: Entered STN: 21 Dec 2003
TITLE: Therapeutic conjugate consisting of a MEK inhibitor and a targeting agent
INVENTOR(S): Lee, Kevin; Ho, Michael Ting Bong
PATENT ASSIGNEE(S): Cambridge Biotechnology Ltd., UK
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K047-48
SECONDARY: A61K047-46
CLASSIFICATION: 63-5 (Pharmaceuticals)
Section cross-reference(s): 14, 15
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003103717	A1	20031218	WO 2003-GB2501	20030611

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2002-13383 A 20020611
ABSTRACT:
Conjugates for use in the treatment of pain, particularly chronic pain are described. The conjugates comprise a MEK inhibitor and a targeting agent. The targeting agent targets the MEK inhibitor to sensory neurons, thereby reducing the dosage of MEK inhibitor required to treat chronic pain. Methods of treating chronic pain using the conjugates are also described.

SUPPL. TERM: analgesic MEK mitogen activated protein kinase inhibitor chronic **pain**
INDEX TERM: Nerve
(A.delta.-fibers; conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)
INDEX TERM: Biological transport
(axonal, facilitators; conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)
INDEX TERM: **Nerve**
(**c-fibers**; conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)
INDEX TERM: Drug delivery systems
(carriers; conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)
INDEX TERM: **Pain**
(chronic; conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)
INDEX TERM: Analgesics
Arthritis

Neoplasm
(conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)

INDEX TERM: Agglutinins and **Lectins**
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)

INDEX TERM: Spinal cord
(dorsal horn; conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)

INDEX TERM: Receptors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(**lectin**, IB4; conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)

INDEX TERM: Antibodies
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal; conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)

INDEX TERM: Nerve, disease
(neuropathy, **pain** from; conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)

INDEX TERM: Inflammation
(**pain** from; conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)

INDEX TERM: Nerve
(sensory, drug targeting to; conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)

INDEX TERM: Drug delivery systems
(targeted; conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)

INDEX TERM: Nerve growth factor receptors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(targeting of; conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)

INDEX TERM: 9061-61-4, Nerve growth factor 109511-58-2D, u0126, conjugates 167869-21-8D, Pd98059, conjugates
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)

INDEX TERM: 142805-58-1, MEK
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):
(1) Alan, F; WO 0057897 A 2000 CAPLUS
(2) Andel Inst van; WO 0217952 A 2002 CAPLUS
(3) Denham, P; WO 0105390 A 2001 CAPLUS
(4) Du Pont Pharm Co; WO 0056706 A 2000 CAPLUS
(5) Du Pont Pharm Co; WO 0056725 A 2000 CAPLUS
(6) Duncia, J; BIOORGANIC & MEDICINAL CHEMISTRY LETTERS 1998, V8(20), P2839 CAPLUS

(7) Ji, R; NATURE NEUROSCIENCE 1999, V2(12), P1114 CAPLUS
(8) John, D; WO 9917806 A 1999 CAPLUS
(9) John, R; WO 9423752 A 1994 CAPLUS
(10) Koo, H; US 2002054869 A1 2002 CAPLUS
(11) Sebolt-Leopold, J; ONCOGENE 2000, V19(56), P6594 CAPLUS
(12) Sezaki, H; CRITICAL REVIEWS IN THERAPEUTIC DRUG CARRIER SYSTEMS 1984, V1, P1 CAPLUS
(13) Takakura, Y; PHARMACEUTICAL RESEARCH 1996, V13(6), P820 CAPLUS

L86 ANSWER 7 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:828902 CAPLUS
DOCUMENT NUMBER: 140:87993
ENTRY DATE: Entered STN: 22 Oct 2003
TITLE: Distribution of antinociceptive adenosine A1 receptors in the spinal cord dorsal horn, and relationship to primary afferents and neuronal subpopulations
AUTHOR(S): Schulte, G.; Robertson, B.; Fredholm, B. B.; DeLander, G. E.; Shortland, P.; Molander, C.
CORPORATE SOURCE: Department of Neuroscience, Karolinska Institutet, Stockholm, SE-171 77, Swed.
SOURCE: Neuroscience (Oxford, United Kingdom) (2003), 121(4), 907-916
CODEN: NRSCDN; ISSN: 0306-4522
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 2-8 (Mammalian Hormones)
ABSTRACT:

Adenosine can reduce pain and allodynia in animals and man, probably via spinal adenosine A1 receptors. In the present study, the authors investigate the distribution of the adenosine A1 receptor in the rat spinal cord dorsal horn using immunohistochem., in situ hybridization, radioligand binding, and confocal microscopy. In the lumbar cord dorsal horn, dense immunoreactivity was seen in the inner part of lamina II. This was unaltered by dorsal root section or thoracic cord hemisection. Confocal microscopy of the dorsal horn revealed close anatomical relationships but no or only minor overlap between A1 receptors and immunoreactivity for markers assocd. with primary afferent central endings: calcitonin gene-related peptide, or isolectin B4, or with neuronal subpopulations: .mu.-opioid receptor, neuronal nitric oxide synthase, met-enkephalin, parvalbumin, or protein kinase C.gamma., or with glial cells: glial fibrillary acidic protein. A few adenosine A1 receptor pos. structures were double-labeled with .alpha.-amino-3-hydroxy-5-methyl-4-isoaxolepropionic acid glutamate receptor subunits 1 and 2/3. The results indicate that most of the adenosine A1 receptors in the dorsal horn are located in inner lamina II postsynaptic neuronal cell bodies and processes whose functional and neurochem. identity is so far unknown. Many adenosine A1 receptor pos. structures are in close contact with isolectin B4 pos. C-fiber primary afferents and/or postsynaptic structures contg. components of importance for the modulation of nociceptive information.

SUPPL. TERM: adenosine A1 receptor **pain** sensory neuron dorsal horn rat
INDEX TERM: Glutamate receptors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(AMPA-binding; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)
INDEX TERM: Adenosine receptors
ROLE: BSU (Biological study, unclassified); BIOL (Biological

study)
(A1; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

NDEX TERM: **Nerve**
(**C-fiber**; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

NDEX TERM: Nerve
(GABAergic; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

NDEX TERM: Glutamate receptors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(GluR1 subunit; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

NDEX TERM: Glutamate receptors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(GluR2 subunit; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

NDEX TERM: Glutamate receptors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(GluR3 subunit; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

NDEX TERM: Nerve
(cell body; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

NDEX TERM: Analgesia
Astrocyte
Pain
(distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

NDEX TERM: Glial fibrillary acidic protein
Parvalbumins
Synaptophysin
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

NDEX TERM: Spinal cord
(dorsal horn; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

NDEX TERM: Agglutinins and **Lectins**
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(isolectins, B4; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and

relationship to primary afferents and neuronal subpopulations)

NDEX TERM: Nerve
(neuron, excitatory- and inhibitory-; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

NDEX TERM: Nerve
(primary sensory; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

NDEX TERM: Opioid receptors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(.mu.-opioid; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

NDEX TERM: 58569-55-4, Met-enkephalin 83652-28-2, Calcitonin gene-related peptide 141436-78-4, Protein kinase C.gamma. 506430-87-1, Neuronal nitric oxide synthase
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

EFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD.

EFERENCE(S):
(1) Aimar, P; J Neurosci 1998, V18, P10375 CAPLUS
(2) Antal, M; J Comp Neurol 1990, V295, P467 CAPLUS
(3) Antal, M; J Comp Neurol 1991, V314, P114 CAPLUS
(4) Arvidsson, U; J Neurosci 1995, V15, P3328 CAPLUS
(5) Bao, L; Eur J Neurosci 2002, V16, P175
(6) Belfrage, M; Anesth Analg 1995, V81, P713 CAPLUS
(7) Carruthers, A; Mol Pharmacol 2001, V59, P1533 CAPLUS
(8) Choca, J; J Pharmacol Exp Ther 1988, V247, P757 CAPLUS
(9) de Koninck, Y; Neurosci Lett 1994, V176, P128 CAPLUS
(10) Delander, G; J Pharmacol Exp Ther 1986, V239, P88 CAPLUS
(11) Dolphin, A; J Physiol 1986, V373, P47 CAPLUS
(12) Ekblom, A; Acta Anaesthesiol Scand 1995, V39, P717 CAPLUS
(13) Geiger, J; J Neurosci 1984, V4, P2303 CAPLUS
(14) Gilmore, S; Glia 1990, V3, P342 MEDLINE
(15) Goodman, R; J Neurosci 1982, V2, P1230 CAPLUS
(16) Gu, J; Nature 1997, V389, P749 CAPLUS
(17) Hajos, F; Neurosci Lett 1990, V117, P8 CAPLUS
(18) Hokfelt, T; Proc Natl Acad Sci USA 1977, V74, P3081 CAPLUS
(19) Holmgren, M; Naunyn Schmiedebergs Arch Pharmacol 1986, V334, P290 CAPLUS
(20) Jo, Y; Nat Neurosci 1999, V2, P241 CAPLUS
(21) Johansson, B; Naunyn Schmiedebergs Arch Pharmacol 1993, V347, P407 CAPLUS
(22) Johansson, B; Proc Natl Acad Sci USA 2001, V98, P9407 CAPLUS
(23) Karlsten, R; Neurosci Lett 1991, V121, P267 CAPLUS
(24) Karlsten, R; Pharmacol Toxicol 1992, V70, P434 CAPLUS
(25) Kemp, T; Neuroscience 1996, V75, P1231 CAPLUS
(26) Lao, L; Pain 2001, V94, P315 CAPLUS
(27) Lee, Y; J Pharmacol Exp Ther 1996, V277, P1642 CAPLUS

(28) Li, J; J Neurophysiol 1994, V72, P1611 CAPLUS
(29) Macdonald, R; J Physiol 1986, V370, P75 CAPLUS
(30) Mahan, L; Mol Pharmacol 1991, V40, P1 CAPLUS
(31) Malmberg, A; Science 1997, V278, P279 CAPLUS
(32) Mauborgne, A; Eur J Pharmacol 2002, V441, P47 CAPLUS
(33) Millan, M; Prog Neurobiol 1999, V57, P1 CAPLUS
(34) Miller, K; J Comp Neurol 1987, V255, P293 CAPLUS
(35) Mori, M; J Comp Neurol 1990, V299, P167 CAPLUS
(36) Polgar, E; Brain Res 1999, V833, P71 MEDLINE
(37) Popratiloff, A; J Neurosci 1996, V16, P3363 CAPLUS
(38) Reeve, A; Br J Pharmacol 1995, V116, P2221 CAPLUS
(39) Reppert, S; Mol Endocrinol 1991, V5, P1037 CAPLUS
(40) Reuss, M; J Chem Neuroanat 2002, V21, P181
(41) Salter, M; Prog Neurobiol 1993, V41, P125 CAPLUS
(42) Santicioli, P; Eur J Pharmacol 1993, V231, P139 CAPLUS
(43) Sawynok, J; Eur J Pharmacol 1998, V347, P1 CAPLUS
(44) Sawynok, J; Pain 1998, V74, P75 CAPLUS
(45) Segerdahl, M; Drug Development Research 1998, V45, P151 CAPLUS
(46) Segerdahl, M; Neuroreport 1995, V6, P753 CAPLUS
(47) Silverman, J; Somatosens Res 1988, V5, P259 MEDLINE
(48) Sjolund, K; Anesth Analg 1997, V85, P627 CAPLUS
(49) Sjolund, K; Eur J Pain 2001, V5, P199 CAPLUS
(50) Spike, R; Eur J Neurosci 1998, V10, P324
(51) Spike, R; Eur J Neurosci 2002, V15, P1306 MEDLINE
(52) Stein, V; Neuron 2003, V37, P375 CAPLUS
(53) Sudhof, T; Nature 1995, V375, P645 MEDLINE
(54) Taiwo, Y; Neuroscience 1990, V38, P757 CAPLUS
(55) Todd, A; Brain Res 1992, V584, P149 CAPLUS
(56) Valtschanoff, J; J Comp Neurol 1992, V321, P209 MEDLINE
(57) Vulchanova, L; Eur J Neurosci 1998, V10, P3470 MEDLINE
(58) Wang, H; Neuroscience 1994, V62, P539 CAPLUS
(59) Woolf, C; J Comp Neurol 1995, V360, P121 MEDLINE
(60) Woolf, C; Nature 1992, V355, P75 MEDLINE
(61) Woolf, C; Pain 1996, V66, P105 MEDLINE
(62) Zhang, X; J Comp Neurol 1993, V335, P563 CAPLUS
(63) Zhang, X; Neuroscience 2000, V95, P197 CAPLUS

L86 ANSWER 8 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:128418 CAPLUS
DOCUMENT NUMBER: 139:255171
ENTRY DATE: Entered STN: 20 Feb 2003
TITLE: Differential response properties of IB4-positive and -negative unmyelinated sensory neurons to protons and capsaicin
AUTHOR(S): Dirajlal, Sahera; Pauers, Laura E.; Stucky, Cheryl L.
CORPORATE SOURCE: Department of Cell Biology, Neurobiology and Anatomy, Medical College of Wisconsin, Milwaukee, WI, 53226-0509, USA
SOURCE: Journal of Neurophysiology (2003), 89(1), 513-524
CODEN: JONEA4; ISSN: 0022-3077
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 1-11 (Pharmacology)
Section cross-reference(s): 13, 14

ABSTRACT:
Activation of unmyelinated (C-fiber) nociceptors by noxious chems. plays a crit. role in the initiation and maintenance of injury-induced pain. C-fiber nociceptors can be divided into two groups in which one class depends on nerve growth factor during postnatal development and contains neuropeptides, and the second class depends on glial cell line-derived neurotrophic factor during

postnatal development and contains few neuropeptides but binds isolectin B4 (IB4). We detd. the sensitivity of these two populations to protons and capsaicin using whole cell recordings of dorsal root ganglion neurons from adult mouse. IB4-neg. unmyelinated neurons were significantly more responsive to protons than IB4-pos. neurons in a concn.-dependent manner. Approx. 86% of IB4-neg. neurons responded to pH 5.0 with an inward current compared with only 33% of IB4-pos. neurons. The subtypes of proton-evoked currents in IB4 neg. unmyelinated neurons were also more diverse. Many IB4 neg. neurons exhibited transient, rapidly inactivating proton currents as well as sustained proton currents. In contrast, IB4 pos. neurons never displayed transient proton currents and responded to protons only with sustained, slowly inactivating inward currents. The two classes of neurons also responded differently to capsaicin. Twice as many naive IB4-neg. unmyelinated neurons responded to 1 .mu.M capsaicin as IB4-pos. neurons, and the capsaicin-evoked currents in IB4 neg. neurons were approx. 4-fold larger than those in IB4 pos. neurons. Interestingly, proton exposure altered the capsaicin responsiveness of the two classes of neurons in opposite ways. Brief pre-exposure to protons increased the no. of capsaicin-responsive IB4-pos. neurons by 2-fold and increased the capsaicin-evoked currents by 3-fold. Conversely, proton exposure decreased the no. of capsaicin-responsive IB4-neg. neurons by 50%. These data suggest that IB4 neg. unmyelinated nociceptors are initially the primary responders to both protons and capsaicin, but IB4-pos. nociceptors have a unique capacity to be sensitized by protons to capsaicin-receptor agonists.

SUPPL. TERM: isolectin B4 receptor unmyelinated sensory neuron proton capsaicin antinociceptive; analgesic capsaicin proton C fiber nociceptor isolectin B4 receptor

INDEX TERM: **Nerve**
(**C-fiber**; differential response properties of isolectin B4-pos. and -neg. unmyelinated sensory neurons to protons and capsaicin)

INDEX TERM: Electric potential
(biol., action; differential response properties of isolectin B4-pos. and -neg. unmyelinated sensory neurons to protons and capsaicin)

INDEX TERM: Analgesics
Pain
(differential response properties of isolectin B4-pos. and -neg. unmyelinated sensory neurons to protons and capsaicin)

INDEX TERM: **Pain** receptors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(differential response properties of isolectin B4-pos. and -neg. unmyelinated sensory neurons to protons and capsaicin)

INDEX TERM: Receptors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(**lectin**, for isolectin B4; differential response properties of isolectin B4-pos. and -neg. unmyelinated sensory neurons to protons and capsaicin)

INDEX TERM: Sodium channel
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(role; differential response properties of isolectin B4-pos. and -neg. unmyelinated sensory neurons to protons and capsaicin)

INDEX TERM: Biological transport
(uptake, of protons; differential response properties of isolectin B4-pos. and -neg. unmyelinated sensory neurons to protons and capsaicin)

INDEX TERM: 12408-02-5, Hydrogen ion, biological studies
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(differential response properties of isolectin B4-pos. and -neg. unmyelinated sensory neurons to protons and capsaicin)

INDEX TERM: 404-86-4, Capsaicin
ROLE: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(differential response properties of isolectin B4-pos. and -neg. unmyelinated sensory neurons to protons and capsaicin)

REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):

(1) Amaya, F; Mol Cell Neurosci 2000, V15, P331 CAPLUS
(2) Averill, S; Eur J Neurosci 1995, V7, P1484 MEDLINE
(3) Babinski, K; J Biol Chem 2000, V275, P28519 CAPLUS
(4) Babinski, K; J Neurochem 1999, V72, P51 CAPLUS
(5) Baumann, T; J Neurosci 2000, V20, P80
(6) Beland, B; Pain 2001, V90, P143 CAPLUS
(7) Bennett, D; Eur J Neurosci 1996, V8, P2204 MEDLINE
(8) Bennett, D; J Neurosci 1998, V18, P3059 CAPLUS
(9) Benson, C; Ann NY Acad Sci 2001, V940, P96 CAPLUS
(10) Benson, C; Proc Natl Acad Sci USA 2002, V99, P2338 CAPLUS
(11) Bevan, S; J Physiol (Lond) 1991, V433, P145 MEDLINE
(12) Caterina, M; Science 2000, V288, P306 CAPLUS
(13) Chen, C; Proc Natl Acad Sci USA 1998, V95, P10240 CAPLUS
(14) Davis, J; Nature 2000, V405, P183 CAPLUS
(15) Djouhri, L; J Physiol (Lond) 1998, V513, P857 CAPLUS
(16) Drew, L; J Neurosci 2002, V22, PRC228
(17) Evans, A; J Physiol (Lond) 1999, V516, P163 CAPLUS
(18) Gillespie, P; Nature 2001, V413, P194 CAPLUS
(19) Griffiths, J; Br J Cancer 1991, V64, P425 CAPLUS
(20) Guler, A; J Neurosci 2002, V22, P6408 CAPLUS
(21) Habler, C; Klin Wochenschr 1929, V8, P1569
(22) Hood, V; Am J Physiol 1988, V255, PF479 MEDLINE
(23) Issberner, U; Neurosci Lett 1996, V208, P191 CAPLUS
(24) Jordt, S; Proc Natl Acad Sci USA 2000, V97, P8134 CAPLUS
(25) Kress, M; Neurosci Lett 1996, V211, P5 CAPLUS
(26) Krishtal, O; Neuroscience 1980, V5, P2325 CAPLUS
(27) Kuzhikandathil, E; J Neurosci 2001, V21, P8697 CAPLUS
(28) Lawson, S; J Physiol (Lond) 1991, V435, P41 MEDLINE
(29) Levine, J; Textbook of Pain (4th ed) 1999, P59
(30) Luger, N; Cancer Res 2001, V61, P4038 CAPLUS
(31) Matsuo, S; Neuroscience 2001, V105, P747 CAPLUS
(32) McCleskey, E; Annu Rev Physiol 1999, V61, P835 CAPLUS
(33) McLatchie, L; Br J Pharmacol 2001, V132, P899 CAPLUS
(34) McMahon, S; Textbook of Pain (4th ed) 1999, P105
(35) Michael, G; J Neurosci 1999, V19, P1844 CAPLUS
(36) Molliver, D; J Comp Neurol 1995, V361, P404 CAPLUS
(37) Molliver, D; Neuron 1997, V19, P849 CAPLUS
(38) Nagy, I; J Neurosci 1999, V19, P10647 CAPLUS
(39) Nagy, J; Neuroscience 1982, V7, P89 CAPLUS
(40) Nicol, G; J Neurophysiol 1997, V77, P167 CAPLUS
(41) Orozco, O; Eur J Neurosci 2001, V13, P2177 MEDLINE
(42) Pan, J; Proc Natl Acad Sci USA 1988, V85, P7836 CAPLUS
(43) Peier, A; Science 2002, V296, P2046 CAPLUS
(44) Perry, M; J Neurocytol 1991, V20, P746 MEDLINE
(45) Petersen, M; Pain 1993, V54, P37 MEDLINE

(46) Price, M; J Biol Chem 1996, V271, P7879 CAPLUS
(47) Price, M; Nature 2000, V407, P1007 MEDLINE
(48) Price, M; Neuron 2001, V32, P1071 CAPLUS
(49) Revici, E; Bull Inst Appl Biol 1949, V1, P21
(50) Ritter, A; J Neurophysiol 1992, V68, P2033 CAPLUS
(51) Shu, X; J Neurophysiol 2001, V86, P2931 CAPLUS
(52) Silverman, J; J Neurocytol 1990, V19, P789 MEDLINE
(53) Smith, G; Nature 2002, V418, P186 CAPLUS
(54) Snider, W; Neuron 1998, V20, P629 CAPLUS
(55) Steen, K; J Neurosci 1992, V12, P86 MEDLINE
(56) Steen, K; Neurosci Lett 1995, V199, P29 CAPLUS
(57) Stucky, C; J Neurosci 1999, V19, P6497 CAPLUS
(58) Tang, C; Science 1988, V240, P213 CAPLUS
(59) Tominaga, M; Neuron 1998, V21, P531 CAPLUS
(60) Vulchanova, L; Neuroscience 2001, V108, P143 CAPLUS
(61) Waldmann, R; Curr Opin Neurobiol 1998, V8, P418 CAPLUS
(62) Waldmann, R; J Biol Chem 1997, V72, P20975
(63) Wang, H; Neuroscience 1994, V62, P539 CAPLUS
(64) Zwick, M; J Neurosci 2002, V22, P4057 CAPLUS

L86 ANSWER 9 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:41375 CAPLUS
DOCUMENT NUMBER: 138:215729
ENTRY DATE: Entered STN: 17 Jan 2003
TITLE: GFR .alpha.2/neurturin signalling regulates noxious heat transduction in isolectin B4-binding mouse sensory neurons
AUTHOR(S): Stucky, Cheryl L.; Rossi, Jari; Airaksinen, Matti S.; Lewin, Gary R.
CORPORATE SOURCE: Growth Factors and Regeneration Group, Department of Neuroscience, Max Delbruck Center for Molecular Medicine, Berlin, D-13092, Germany
SOURCE: Journal of Physiology (Cambridge, United Kingdom) (2002), 545(1), 43-50
CODEN: JPHYA7; ISSN: 0022-3751
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 2-10 (Mammalian Hormones)
ABSTRACT:

The GFR .alpha.2 receptor is the cognate co-receptor for the neurotrophic factor neurturin and GFR .alpha.2 is selectively expressed by isolectin B4 (IB4)-binding nociceptive sensory neurons. Here, the authors used two physiol. approaches in combination with mice that have a targeted deletion of the GFR .alpha.2 gene (GFR .alpha.2 -/- mice) to det. whether GFR .alpha.2/neurturin signaling regulates the functional properties or the survival of IB4-binding nociceptors. Because 50% of IB4-binding neurons respond to noxious heat and because patch clamp recordings of isolated dorsal root ganglion sensory neurons allow one to neurochem. identify subpopulations of neurons, the authors analyzed the noxious heat responsiveness of IB4-pos. and -neg. small-diam. neurons isolated from adult GFR .alpha.2 -/- and littermate control mice. The percentage of IB4-pos. neurons that had large (> 100 pA) heat-evoked inward currents was severely reduced in GFR .alpha.2 -/- mice (12%) compared to wild-type littermates (47%), and this loss in large-magnitude heat currents was accounted for by an increase in neurons with very small (< 100 pA) heat-evoked currents as well as an increase in neurons with no detectable heat current. Counts of IB4-pos. and -neg. neurons, as well as counts of unmyelinated axons in the saphenous nerve, confirmed that the loss in neurons with large-amplitude heat currents was due to a deficit in heat transduction and not a decrease in cell survival. The effect was modality specific for heat because mech. transduction of all fiber types, including IB4-pos. C fibers, was normal. The authors' data are the first to indicate a transduction-function role for GFR

alpha.2/neurturin signaling in a specific class of sensory neurons.

UPPL. TERM: neurotrophic factor receptor GFR alpha heat signaling isolectin B4; **pain** receptor skin signaling isolectin B4 sensory neuron mouse

NDEX TERM: **Nerve**
(**C-fiber**; GFR .alpha.2/neurturin signaling regulates noxious heat transduction in isolectin B4-binding mouse sensory neurons)

NDEX TERM: **Pain**
Signal transduction, biological
(GFR .alpha.2/neurturin signaling regulates noxious heat transduction in isolectin B4-binding mouse sensory neurons)

NDEX TERM: **Pain** receptors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(GFR .alpha.2/neurturin signaling regulates noxious heat transduction in isolectin B4-binding mouse sensory neurons)

NDEX TERM: Neurotrophic factor receptors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(GFR-.alpha.2; GFR .alpha.2/neurturin signaling regulates noxious heat transduction in isolectin B4-binding mouse sensory neurons)

NDEX TERM: Axon
(diam.; GFR .alpha.2/neurturin signaling regulates noxious heat transduction in isolectin B4-binding mouse sensory neurons)

NDEX TERM: Temperature effects, biological
(heat, noxious; GFR .alpha.2/neurturin signaling regulates noxious heat transduction in isolectin B4-binding mouse sensory neurons)

NDEX TERM: Agglutinins and **Lectins**
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(isolectins, B4; GFR .alpha.2/neurturin signaling regulates noxious heat transduction in isolectin B4-binding mouse sensory neurons)

NDEX TERM: Nerve
(myelinated; GFR .alpha.2/neurturin signaling regulates noxious heat transduction in isolectin B4-binding mouse sensory neurons)

NDEX TERM: Skin
(sensory neuron; GFR .alpha.2/neurturin signaling regulates noxious heat transduction in isolectin B4-binding mouse sensory neurons)

NDEX TERM: Nerve
(sensory, skin; GFR .alpha.2/neurturin signaling regulates noxious heat transduction in isolectin B4-binding mouse sensory neurons)

NDEX TERM: 185857-51-6, Neurturin
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(GFR .alpha.2/neurturin signaling regulates noxious heat transduction in isolectin B4-binding mouse sensory neurons)

EFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD.

EFERENCE(S): (1) Baloh, R; Current Opinion in Neurobiology 2000, V10, P103 CAPLUS

(2) Bennett, D; Journal of Neuroscience 1998, V18, P3059 CAPLUS
(3) Caterina, M; Nature 1997, V389, P816 CAPLUS
(4) Caterina, M; Science 2000, V288, P306 CAPLUS
(5) Cellerino, A; Molecular and Cellular Neuroscience 1997, V9, P397 CAPLUS
(6) Chuang, H; Nature 2001, V411, P957 CAPLUS
(7) Davis, J; Nature 2000, V405, P183 CAPLUS
(8) Garces, A; Journal of Neuroscience 2000, V20, P4992 CAPLUS
(9) Gerke, M; Brain Research 2001, V911, P101 CAPLUS
(10) Guler, A; Journal of Neuroscience 2002, V22, P6408 CAPLUS
(11) Heppenstall, P; Current Opinion in Anaesthesiology 2000, V13, P573
(12) Heuckeroth, R; Neuron 1999, V22, P253 CAPLUS
(13) Koltzenburg, M; Journal of Neurophysiology 1997, V78, P1841 MEDLINE
(14) Kress, M; Journal of Neurophysiology 1992, V68, P581 MEDLINE
(15) Molliver, D; Neuron 1997, V19, P849 CAPLUS
(16) Peier, A; Science 2002, V296, P2046 CAPLUS
(17) Pesquero, J; Proceedings of the National Academy of Sciences of the USA 2000, V97, P8140 CAPLUS
(18) Rossi, J; Neuron 1999, V22, P243 CAPLUS
(19) Shu, X; Journal of Neurophysiology 2001, V86, P2931 CAPLUS
(20) Shu, X; Neuroscience Letters 1999, V274, P159 CAPLUS
(21) Smith, G; Nature 2002, V418, P186 CAPLUS
(22) Snider, W; Neuron 1998, V20, P629 CAPLUS
(23) Stucky, C; Journal of Neuroscience 1999, V19, P6497 CAPLUS
(24) Stucky, C; Journal of Neuroscience 1999, V19, P8509 CAPLUS
(25) Vulchanova, L; Neuroscience 2001, V108, P143 CAPLUS
(26) Zwick, M; Journal of Neuroscience 2002, V22, P4057 CAPLUS

L86 ANSWER 10 OF 26 DRUGU COPYRIGHT 2004 THOMSON DERWENT on STN DUPLICATE 2
ACCESSION NUMBER: 2003-12380 DRUGU P
TITLE: Inhibition of release of neurotransmitters from rat dorsal root ganglia by a novel conjugate of a Clostridium botulinum toxin A endopeptidase fragment and **Erythrina cristagalli lectin**.
AUTHOR: Duggan M J; Quinn C P; Chaddock J A; Purkiss J R; Alexander F C G; Doward S J F; Fooks S J; Friis L M; Hall Y H J; Kirby E R
CORPORATE SOURCE: Centre-App.Micro+Res.Porton-Down; Univ.London
LOCATION: Salisbury; London, U.K.
SOURCE: J.Biol.Chem. (277, No. 38, 34846-52, 2002) 4 Fig. 34 Ref.
CODEN: JBCHA3 ISSN: 0021-9258
AVAIL. OF DOC.: Center for Applied Microbiology and Research, Porton Down, Salisbury, Wiltshire SP4 0JG, England. (J.A.C., 18 authors). (e-mail: john.chaddock@camr.org.uk).
LANGUAGE: English
DOCUMENT TYPE: Journal

ABSTRACT:

The catalytically active derivative (LHN) of the type A neurotoxin from Clostridium botulinum was coupled to a **lectin** obtained from ***Erythrina*** **cristagalli** (ECL, Sigma-Chem.) to form a novel

conjugate. Chemical conjugates prepared between ECL and either native (n) or recombinant (r) LHN inhibited substance P release from embryonic dorsal root ganglia (eDRG) and glycine from embryonic spinal cord **neuron** (eSCN).The dependence of inhibition of neurotransmitter release on the cleavage of SNAP-25 was shown through the use of an endopeptidase-deficient LHN conjugate variant. The duration of action of inhibition of neurotransmitter released by the LHN-ECL in-vitro was similar to that seen with C. botulinum neurotoxin (BT). These findings suggest that the inhibition of release of neurotransmitters from a **neuronal** population of therapeutic relevance to the treatment of pain can be achieved.

SECTION HEADING: P Pharmacology

CLASSIF. CODE: 60 Autonomic

CONTROLLED TERM:
NEURON *FT; GANGLION *FT; TISSUE-CULTURE *FT; IN-VITRO *FT; SNAP-25 *FT; COUPLING *FT; GLYCINE *FT; AMINOACID-METAB. *FT; MOUSE *FT; IN-VIVO *FT; CLEAVAGE *FT; CONJUGATE *FT; INTRATHECAL *FT; I.P. *FT; LAB.ANIMAL *FT; INJECTION *FT
[01] SIGMA-CHEM. *FT; **LECTIN** *FT; **ERYTHRINA** *FT; CRYSTAGALLI *FT; PH *FT
[02] BOTULINUM-A-TOXIN *PH; BOTULATOX *RN; NATIVE *FT; RECOMBINANT *FT; SPASMOLYTICS *FT; TOXINS *FT; PH *FT
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L86 ANSWER 11 OF 26 DRUGU COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-27692 DRUGU A S
TITLE: Characterisation of a novel conjugate of a botulinum neurotoxin A endopeptidase fragment and E. **cristagalli lectin**.
AUTHOR: Ling R J; Fretwell R; Alexander F; Fooks S; Leeds N; Jameson K; Hall Y; Kirby E; Chaddock J; Stone C
LOCATION: Salisbury, U.K.
SOURCE: Arch.Pharmacol. (365, Suppl. 2, R28, 2002) 1 Ref.
CODEN: NSAPCC ISSN: 0028-1298
AVAIL. OF DOC.: Centre for Applied Microbiology and Research, Porton Down, Salisbury, Wiltshire, SP4 OJG, England.
LANGUAGE: English
DOCUMENT TYPE: Journal

ABSTRACT:

The aim of this study was to prepare novel molecules with a selectivity for nociceptive **neurons**. Using the 2-domain LHn fragment of BoNT/A or recombinant recLHn/A, conjugates were prepared with a Coral Tree **lectin** (**Erythrina cristagalli**: ECL). A much improved toxicity profile in mice was demonstrated for the conjugates compared to the whole toxin. In-vitro in **neuronal** cultures in-vitro, the equivalency of the recLHn/A-ECL and the nLHn/A-ECL conjugates were demonstrated. These data represent an important step forward in the pursuit of establishing the therapeutic potential of retargeted endopeptidases. (conference abstract: International Conference on Basic and Therapeutic Aspects of Botulinum and Tetanus Toxins, Hannover, Germany, 2002).

SECTION HEADING: A Analysis
S Adverse Effects

CLASSIF. CODE: 34 Toxicology
59 CNS and Motor

65 Drug Delivery
70 Analysis

CONTROLLED TERM:
[01] IN-VITRO *FT; TOX. *FT; CONJUGATE *FT; **LECTIN** *FT; IN-VIVO *FT; MOUSE *FT; TARGETING *FT; **NEURON** *FT; LAB.ANIMAL *FT; DRUG-DELIVERY *FT; OC *FT; AE *FT
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L86 ANSWER 12 OF 26 DRUGU COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-27671 DRUGU P S
TITLE: Retargeted clostridial endopeptidase: antinociceptive activity in preclinical models of pain.
AUTHOR: Cui M; Chaddock J A; Rubino J; Khanijou S; Duggan M J; Walsh B; Foster K A; Aoki K R
CORPORATE SOURCE: Allergan
LOCATION: Irvine, Cal., USA; Salisbury, U.K.
SOURCE: Arch.Pharmacol. (365, Suppl. 2, R16, 2002)
CODEN: NSAPCC ISSN: 0028-1298
AVAIL. OF DOC.: Allergan Inc., 2525 Dupont Drive, Irvine, CA92612, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal

ABSTRACT:

A fragment of botulinum neurotoxin A lacking the binding domain (LHn/A) was chemically conjugated to **Erythrina cristagalli** ***lectin*** (ECL) to produce LNn/A-ECL. This conjugate was tested following i.t. and s.c. administration in the murine hot plate model, rat formalin model and Chung model (all models of acute pain). The results showed that LHn/A-ECL is a novel agent designed to selectively deliver the endopeptidase activity of botulinum neurotoxin to nociceptive afferent **neurons**. It displayed long-lasting analgesic properties in a range of in-vivo models of pain. LHn/A-ECL did not produce any muscle weakness. (conference abstract: International Conference on Basic and Therapeutic Aspects of Botulinum and Tetanus Toxins, Hannover, Germany, 2002).

SECTION HEADING: P Pharmacology
S Adverse Effects

CLASSIF. CODE: 34 Toxicology
43 Analgesics, NSAIDs
65 Drug Delivery

CONTROLLED TERM:
[01] PAIN *OC; INTRATHECAL *FT; S.C. *FT; IN-VIVO *FT; RAT *FT; MOUSE *FT; ANALGESIC *FT; CONJUGATE *FT; DRUG-DELIVERY *FT; SIDE-EFFECT-ABSENT *FT; ANIMAL-MODEL *FT; LAB.ANIMAL *FT; PH *FT; AE *FT
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L86 ANSWER 13 OF 26 PASCAL COPYRIGHT 2004 INIST-CNRS. ALL RIGHTS RESERVED. on STN DUPLICATE 1
ACCESSION NUMBER: 2004-0228708 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 2004 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): Retargeted clostridial endopeptidases: Inhibition of nociceptive neurotransmitter release in vitro, and antinociceptive activity in in vivo models of pain
Basic and Therapeutic Aspects of Neurotoxins

JTHOR: CHADDOCK John A.; PURKISS John R.; ALEXANDER Frances C. G.; DOWARD Sarah; FOOKS Sarah J.; FRIIS Lorna M.; HALL Yper H. J.; KIRBY Elizabeth R.; LEEDS Nicola; MOULSDALE Hilary J.; DICKENSON Anthony; GREEN G. Mark; RAHMAN Wahida; SUZUKI Rie; DUGGAN Michael J.; QUINN Conrad P.; SHONE Clifford C.; FOSTER Keith A. BIGALKE HANS (ed.); DRESSLER Dirk (ed.); JANKOVIC Joseph (ed.)

ORPORATE SOURCE: Health Protection Agency, Porton Down, Salisbury, Wiltshire, United Kingdom; University College London, University College, Gower Street, London, United Kingdom
Institute of Toxicology, Medical School of Hannover, Hannover, Germany, Federal Republic of; Department of Neurology, Rostock University, Rostock, Germany, Federal Republic of; Parkinson's Disease Center and Movement Disorders Clinic, Department of Neurology, Baylor College of Medicine, Houston, Texas, United States

OURCE: Movement disorders, (2004), 19(SUP8), 42-47, 22 refs.
Conference: Toxins 2002. Conference, Hannover (Germany, Federal Republic of), 2002
ISSN: 0885-3185

OCUMENT TYPE: Journal; Conference
IBLIOGRAPHIC LEVEL: Analytic
OUNTRY: United States
ANGUAGE: English
VAILABILITY: INIST-20953, 354000113591720060

BSTRACT: Clostridial neurotoxins potently and specifically inhibit neurotransmitter release in defined cell types. Previously reported data have demonstrated that the catalytically active LH.sub.N endopeptidase fragment of botulinum neurotoxin type A (termed LH.sub.N/A) can be retargeted to a range of cell types in vitro to lead to inhibition of secretion of a range of transmitters. Here, we report the synthesis of endopeptidase conjugates with in vitro selectivity for nociceptive afferents compared to spinal **neurons**. Chemical conjugates prepared between **Erythrina cristagalli lectin** and LH.sub.N/A are assessed in vitro and in in vivo models of pain. Chemical conjugates prepared between E. **cristagalli lectin** and either natively sourced LH.sub.N/A. or recombinant LH.sub.N/A purified from Escherichia coli are assessed, and equivalence of the recombinant material is demonstrated. The duration of action of inhibition of neurotransmitter release by the conjugate in vitro is also assessed and is comparable to that observed with Clostridium botulinum neurotoxin. Selectivity of targeting and therapeutic potential have been confirmed by in vivo electrophysiology studies. Furthermore, the analgesic properties of the conjugate have been assessed in in vivo models of pain and extended duration effects observed. These data provide proof of principle for the concept of retargeted clostridial endopeptidases as novel analgesics.

LASSIFICATION CODE: 002B17; Life sciences; Medical sciences; Neurology, Nervous system

ONTROLLED TERM: Nervous system diseases; Endopeptidase; Neuromediator; Neurotransmitter; Biological activity; Pain

ROADER TERM: Peptidases; Hydrolases; Enzyme

L86 ANSWER 14 OF 26 PASCAL COPYRIGHT 2004 INIST-CNRS. ALL RIGHTS RESERVED.
on STN DUPLICATE 7

ACCESSION NUMBER: 1995-0359246 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 1995 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): **Lectin** and immunohistochemical comparison of glycoconjugates in the conjunctiva of patients with and without exfoliation syndrome
AUTHOR: HIETANEN J.; UUSITALO M.; TARKKANEN A.; KIVELAE T.
CORPORATE SOURCE: Helsinki univ. cent. hosp., dep. ophthalmology, 00290 Helsinki, Finland
SOURCE: British journal of ophthalmology, (1995), 79(5), 467-472, 33 refs.
ISSN: 0007-1161 CODEN: BJOPAL
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United Kingdom
LANGUAGE: English
AVAILABILITY: INIST-1015, 354000050929870160
ABSTRACT: Aims-The study was carried out to search for labelling similar to that of intraocular exfoliation material in the conjunctiva by light microscopy using **lectin** and immunohistochemistry. Methods-Ten formalin fixed and paraffin embedded conjunctival biopsy specimens both from patients with and without exfoliation syndrome were studied with a panel of 11 **lectins** and with three monoclonal antibodies to the HNK-1 carbohydrate epitope, all of which react with intraocular exfoliation material. Results-The **lectin** binding profile was essentially the same in specimens from patients with and without exfoliation syndrome. The superficial epithelium reacted similarly with Phaseolus vulgaris (PHA-E), Caragana arborescens (CAA), Helix pomatia (HPA), concanavalin A (ConA), and wheat germ (WGA) agglutinins. Binding was also detected with peanut (PNA) and Bauhinia purpurea (BPA) agglutinins, particularly in patients with exfoliation. The basement membrane generally reacted with Ricinus communis (RCA-I), PHA-E, Vicia villosa (VVA), ConA, and Lens culinaris (LCA) agglutinins. The stroma was weakly labelled with RCA-I, PHA-E, ConA, and LCA. **Lectin** binding to the vascular endothelium was moderate with RCA-I, PHA-E, CAA, ConA, LCA, and WGA. Inconsistent labelling was also detected with PNA, BPA, and **Erythrina cristagalli** agglutinin (ECA). The subendothelial region reacted weakly but consistently with PHA-E, ConA, and LCA, and inconsistently with PNA. Pretreatment with neuraminidase did not change that pattern. Antibodies to the HNA-I epitope reacted only with myelinated stromal **nerve** branches. Conclusion-No evidence of abnormal deposits in any specimen was found. The carbohydrate composition of intraocular exfoliation material may differ from that of exfoliation-like fibres often detected in the conjunctiva by electron microscopy
CLASSIFICATION CODE: 002B09G; Life sciences; Medical sciences; Ophthalmology
CONTROLLED TERM: Exfoliation; Lens; Immunohistochemistry; **Lectin**; Glycoconjugate; Conjunctiva; Optical

microscopy; Exploration; Human
BROADER TERM: Eye disease; Lens disease; Pathology

L86 ANSWER 15 OF 26 Elsevier BIOBASE COPYRIGHT 2004 Elsevier Science B.V. on STN DUPLICATE

ACCESSION NUMBER: 1998221674 ESBIOBASE
TITLE: **Lectin** binding patterns in the vomeronasal organ and accessory olfactory bulb of the rat
AUTHOR: Salazar I.; Sanchez Quinteiro P.
CORPORATE SOURCE: I. Salazar, Departamento Anatomia y Embriologia, Facultad de Veterinaria de Lugo, Universidad Santiago de Compostela, E-27002 Lugo, Spain.
E-mail: anigsabe@lugo usc.es
SOURCE: Anatomy and Embryology, (1998), 198/4 (331-339), 55 reference(s)
CODEN: ANEMDG ISSN: 0340-2061
DOCUMENT TYPE: Journal; Article
COUNTRY: Germany, Federal Republic of
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT: A number of previous studies have indicated that **lectin** histochemistry is an obvious choice for characterizing the vomeronasal system. However, apparently inconsistent results have been obtained: notably, the affinity with which various **lectins** bind to the accessory olfactory bulb varies among taxa, even considering closely related species. In the present study, the binding patterns of seven **lectins** in the rat accessory olfactory bulb, vomeronasal **nerves** and vomeronasal duct were investigated. The Bandeiraea simplicifolia **lectin** bound exclusively to the vomeronasal **nerve** and glomerular layers of the accessory olfactory bulb, while the Ulex europeus and Lycopersicon esculentum **lectins** bound to these regions and additionally to the **nerve** and glomerular layers of the main olfactory bulb. Soybean agglutinin showed a similar pattern to that obtained with the Ulex europeus and Lycopersicon esculentum **lectins**, though it also faintly labelled other parts of the structures examined. The Vicia villosa and **Erythrina cristagalli lectins** were not specific for the vomeronasal system, since they labelled grey and white matters in structures including the lateral olfactory tract and the anterior olfactory nuclei. The Dolichos biflorus **lectin** did not bind to vomeronasal tissues. The observed patterns of binding in the accessory olfactory bulb were consistent with those observed in the vomeronasal **nerves**, but unlike those observed in the epithelium of the vomeronasal duct. This latter result probably reflects binding of **lectins** to sugar residues contained in secreted mucus rather than those in epithelial **nerve** endings.
CLASSIFICATION CODE: 88.4.14 NEUROSCIENCE: PHYSIOLOGY OF THE CENTRAL NERVOUS SYSTEM: Olfactory Bulb
SUPPLEMENTARY TERM: Accessory olfactory bulb; Vomeronasal epithelium; Vomeronasal **nerves**; Glycoproteins; Rat

L86 ANSWER 16 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 4

ACCESSION NUMBER: 2000:374003 BIOSIS
DOCUMENT NUMBER: PREV200000374003
TITLE: Role of neurotrophins and **lectins** in prevention of ototoxicity.
AUTHOR(S): Gao, Wei-Qiang [Reprint author]
CORPORATE SOURCE: Department of Neuroscience, Genentech, Inc., 1 DNA Way, South San Francisco, CA, 94080, USA
SOURCE: Henderson, Donald; Salvi, Richard J.; Quaranta, Antonio; McFadden, Sandra L.; Burkard, Robert F. Ann. N. Y. Acad. Sci., (1999) pp. 312-327. Annals of the New York Academy of Sciences. print.
Publisher: New York Academy of Sciences, 2 East 63rd Street, New York, NY, 10021, USA. Series: Annals of the New York Academy of Sciences.
Meeting Info.: Conference on Ototoxicity: Basic Science and Clinical Applications. Bari, Italy. June 18-20, 1999.
CODEN: ANYAA9. ISSN: 0077-8923. ISBN: 1-57331-204-5 (cloth), 1-57331-205-3 (paper).
DOCUMENT TYPE: Book
Conference; (Meeting)
Book; (Book Chapter)
Conference; (Meeting Paper)
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Aug 2000
Last Updated on STN: 8 Jan 2002
CONCEPT CODE: Biochemistry studies - General 10060
General biology - Symposia, transactions and proceedings 00520
Cytology - Animal 02506
Biochemistry studies - Proteins, peptides and amino acids 10064
Endocrine - Neuroendocrinology 17020
Sense organs - Physiology and biochemistry 20004
Sense organs - Pathology 20006
Nervous system - Physiology and biochemistry 20504
Toxicology - General and methods 22501
Tissue culture, apparatus, methods and media 32500
INDEX TERMS: Major Concepts
Sense Organs (Sensory Reception); Toxicology
INDEX TERMS: Parts, Structures, & Systems of Organisms
cochlea: sensory system, explant culture; hair cells: nervous system, sensory system, degeneration; spiral ganglion **neurons**: nervous system, degeneration
INDEX TERMS: Diseases
hearing loss: ear disease, toxicity, ototoxin-induced Hearing Disorders (MeSH)
INDEX TERMS: Diseases
ototoxicity: ear disease, toxicity
INDEX TERMS: Chemicals & Biochemicals
Detura stramonium **lectin**; **Erythrina cristagalli lectin**; brain derived neurotrophic factor [BDNF]; cisplatin: ototoxin; concanavalin A [Con A]: **lectin**, ototoxicity protective effects; gentamicin: ototoxin; neurotrophin-3 [NT-3]; neurotrophin-4/5 [NT-4/5]; sodium salicylate: ototoxin
INDEX TERMS: Miscellaneous Descriptors
Book Chapter; Meeting Paper
ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia

Searched by Barb O'Bryen, STIC 571-272-2518

Organism Name
rat
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

REGISTRY NUMBER: 15663-27-1 (cisplatin)
11028-71-0 (concanavalin A)
11028-71-0 (Con A)
1403-66-3 (gentamicin)
130939-66-1 (neurotrophin-3)
130939-66-1 (NT-3)
54-21-7 (sodium salicylate)

L86 ANSWER 17 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 8
ACCESSION NUMBER: 1991:184067 BIOSIS
DOCUMENT NUMBER: PREV199191098816; BA91:98816
TITLE: **LECTIN** LOCALIZATION IN HUMAN **NERVE** BY BIOCHEMICALLY DEFINED **LECTIN**-BINDING GLYCOPROTEINS NEOGLYCOPROTEIN AND **LECTIN**-SPECIFIC ANTIBODY.
AUTHOR(S): GABIUS H-J [Reprint author]; WOSGIEN B; HENDRYS M; BARDOSI A
CORPORATE SOURCE: MAX-PLANCK-INSTITUT FUR EXPERIMENTELLE MEDIZIN, ABTEILUNG CHEMIE, HERMANN-REIN-STRASSE 3, W-3400 GOETTINGEN
SOURCE: Histochemistry, (1991) Vol. 95, No. 3, pp. 269-278.
CODEN: HCMYAL. ISSN: 0301-5564.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 19 Apr 1991
Last Updated on STN: 19 Apr 1991

ABSTRACT:Molecular recognition can be mediated by protein (**lectin**)-carbohydrate interaction, explaining the interest in this topic. Plant ***lectins*** and, more recently, chemically glycosylated neoglycoproteins principally allow to map the occurrence of components of this putative recognition system. Labelled endogenous **lectins** and the ***lectin*** -binding ligands can add to the panel of glycohistochemical tools. They may be helpful to derive physiologically valid conclusions in this field for mammalian tissues. Consequently, experiments were prompted to employ the abundant .beta.-galactoside-specific **lectin** of human ***nerves*** in affinity chromatography and in histochemistry to purify and to localize its specific glycoprotein ligands. In comparison to the .beta.-galactoside-specific plant **lectins** from Ricinus communis and ***Erythrina*** **cristagalli**, notable similarites were especially detectable in the respective profiles of the mammalian and the ***Erythrina*** **lectin**. They appear to account for rather indistinguishable staining patterns in fixed tissue sections. Inhibitory controls within affinity chromatography, within solid-phase assays for each fraction of **lectin**-binding glycoproteins and within histochemistry as well as the demonstration of crossreactivity of the three fractions of ***lectin*** -binding glycoproteins with the biotinylated **Erythrina** ***lectin*** in blotting ascertained the specificity of the **lectin** -glycoprotein interaction. In addition to monitoring the accessible cellular ligand part by the endogenous **lectin** as probe, the comparison of immunohistochemical and glycohistochemical detection of the **lectin** in serial sections proved these methods for receptor analysis to be rather equally effective. The observation that the bioytinylated **lectin**-binding glycoproteins are also appropriate ligands in glycohistochemical analysis warrants emphasis. Overall, the introduction of biotinylated mammalian ***lectins*** as well as the **lectin**-binding glycoproteins will aid to critically evaluate the physiological significance of the glycobiological

interplay between endogenous **lectins** and distinct carbohydrate parts of cellular glycoconjugates.

CONCEPT CODE: Microscopy - Histology and histochemistry 01056
Cytology - Human 02508
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Carbohydrates 10068
Nervous system - Physiology and biochemistry 20504
Immunology - General and methods 34502
Plant physiology - Chemical constituents 51522

INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Immune System (Chemical Coordination and Homeostasis); Methods and Techniques; Nervous System (Neural Coordination)

INDEX TERMS: Miscellaneous Descriptors
MOLECULAR RECOGNITION CELLULAR GLYCOCONJUGATE IMMUNOHISTOCHEMISTRY

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

L86 ANSWER 18 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:520045 BIOSIS
DOCUMENT NUMBER: PREV200200520045
TITLE: Retargeted endopeptidase-dependent inhibition of neurotransmitters from **neurons** involved in nociception.
AUTHOR(S): Moulsdale, H. J. [Reprint author]; Hall, Y. [Reprint author]; Kirby, E. R. [Reprint author]; Purkiss, J. R. [Reprint author]; Chaddock, J. A. [Reprint author]; Foster, K. A. [Reprint author]
CORPORATE SOURCE: Centre for Applied Microbiology and Research, Porton Down, Salisbury, Wiltshire, SP4 0JG, UK
SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology, (June, 2002) Vol. 365, No. Supplement 2, pp. R30. print.
Meeting Info.: International Conference on Basic and Therapeutic Aspects of Botulinum and Tetanus Toxins. Hannover, Germany. June 08-12, 2002.
CODEN: NSAPCC. ISSN: 0028-1298.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Oct 2002
Last Updated on STN: 9 Oct 2002

CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Cytology - Animal 02506
Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids 10064
Nervous system - Physiology and biochemistry 20504

INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Nervous System (Neural Coordination)

INDEX TERMS: Parts, Structures, & Systems of Organisms
dorsal root ganglia: nervous system; **neurons**: nervous system; spinal cord: nervous system

INDEX TERMS: Chemicals & Biochemicals
Erythrina cristagalli lectin
; botulinum neurotoxin A; calcitonin gene related peptide: neurotransmitter; endopeptidase; glutamate: amino acid, neurotransmitter; substance P: neurotransmitter
INDEX TERMS: Miscellaneous Descriptors
nociception; Meeting Abstract
REGISTRY NUMBER: 83652-28-2 (calcitonin gene related peptide)
9001-92-7 (endopeptidase)
11070-68-1 (glutamate)
33507-63-0 (substance P)

L86 ANSWER 19 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:520037 BIOSIS
DOCUMENT NUMBER: PREV200200520037
TITLE: Characterisation of a novel conjugate of a botulinum neurotoxin A endopeptidase fragment and E. **cristagalli lectin.**
AUTHOR(S): Ling, R. J. [Reprint author]; Fretwell, R.; Alexander, F.; Fooks, S.; Leeds, N.; Jameson, K.; Hall, Y.; Kirby, E.; Chaddock, J.; Shone, C.
CORPORATE SOURCE: Centre for Applied Microbiology and Research, Porton Down, Salisbury, Wiltshire, SP4 0JG, UK
SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology, (June, 2002) Vol. 365, No. Supplement 2, pp. R28. print.
Meeting Info.: International Conference on Basic and Therapeutic Aspects of Botulinum and Tetanus Toxins. Hannover, Germany. June 08-12, 2002.
CODEN: NSAPCC. ISSN: 0028-1298.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Oct 2002
Last Updated on STN: 9 Oct 2002
CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Cytology - General 02502
Cytology - Animal 02506
Enzymes - General and comparative studies: coenzymes 10802
Nervous system - Physiology and biochemistry 20504
INDEX TERMS: Major Concepts
Cell Biology; Enzymology (Biochemistry and Molecular Biophysics); Nervous System (Neural Coordination)
INDEX TERMS: Parts, Structures, & Systems of Organisms
neurons: nervous system, nociceptive
INDEX TERMS: Chemicals & Biochemicals
Erythrina cristagalli lectin
; botulinum neurotoxin A; botulinum neurotoxin A endopeptidase: fragment
INDEX TERMS: Miscellaneous Descriptors
Meeting Abstract

L86 ANSWER 20 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:520029 BIOSIS
DOCUMENT NUMBER: PREV200200520029
TITLE: The extended duration of action of retargeted endopeptidase in embryonic dorsal root ganglia **neurons**.
AUTHOR(S): Kirby, E. R. [Reprint author]; Moulsdale, H. J. [Reprint author]; Hall, Y. [Reprint author]; Chaddock, J. A. [Reprint author]; Foster, K. A. [Reprint author]

CORPORATE SOURCE: Centre for Applied Microbiology and Research, Porton Down, Salisbury, Wiltshire, SP4 0JG, UK
SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology, (June, 2002) Vol. 365, No. Supplement 2, pp. R26. print.
Meeting Info.: International Conference on Basic and Therapeutic Aspects of Botulinum and Tetanus Toxins. Hannover, Germany. June 08-12, 2002.
CODEN: NSAPCC. ISSN: 0028-1298.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Oct 2002
Last Updated on STN: 9 Oct 2002
CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Cytology - General 02502
Cytology - Animal 02506
Biochemistry studies - Proteins, peptides and amino acids 10064
Enzymes - General and comparative studies: coenzymes 10802
Nervous system - Physiology and biochemistry 20504
INDEX TERMS: Major Concepts
Cell Biology; Enzymology (Biochemistry and Molecular Biophysics); Nervous System (Neural Coordination)
INDEX TERMS: Parts, Structures, & Systems of Organisms
dorsal root ganglia **neurons**: nervous system, culture, embryonic
INDEX TERMS: Chemicals & Biochemicals
Erythrina cristagalli lectin
[substance P]; SNAP-25; botulinum neurotoxin A; endopeptidase
INDEX TERMS: Miscellaneous Descriptors
Meeting Abstract
REGISTRY NUMBER: 9001-92-7 (endopeptidase)
33507-63-0 (SUBSTANCE P)

L86 ANSWER 21 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:519991 BIOSIS
DOCUMENT NUMBER: PREV200200519991
TITLE: Retargeted clostridial endopeptidase: Antinociceptive activity in preclinical models of pain.
AUTHOR(S): Cui, M. [Reprint author]; Chaddock, J. A.; Rubino, J. [Reprint author]; Khanijou, S. [Reprint author]; Duggan, M. J.; Walsh, B.; Foster, K. A.; Aoki, K. R. [Reprint author]
CORPORATE SOURCE: Allergan Inc., 2525 Dupont Drive, Irvine, CA, 92612, USA
SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology, (June, 2002) Vol. 365, No. Supplement 2, pp. R16. print.
Meeting Info.: International Conference on Basic and Therapeutic Aspects of Botulinum and Tetanus Toxins. Hannover, Germany. June 08-12, 2002.
CODEN: NSAPCC. ISSN: 0028-1298.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Oct 2002
Last Updated on STN: 9 Oct 2002
CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Cytology - Animal 02506
Biochemistry studies - Proteins, peptides and amino acids 10064

Enzymes - General and comparative studies: coenzymes 10802
Pathology - Therapy 12512
Nervous system - Physiology and biochemistry 20504
Nervous system - Pathology 20506
Pharmacology - General 22002

INDEX TERMS: Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Nervous System (Neural Coordination); Pharmaceuticals (Pharmacology)

INDEX TERMS: Parts, Structures, & Systems of Organisms
sensory **neurons**: nervous system

INDEX TERMS: Diseases
neuropathic pain: nervous system disease
Pain (MeSH)

INDEX TERMS: Diseases
pain: nervous system disease
Pain (MeSH)

INDEX TERMS: Chemicals & Biochemicals
Erythrina cristagalli lectin
: protein; botulinum toxin A; endopeptidase

INDEX TERMS: Miscellaneous Descriptors
Meeting Abstract

ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
mouse: animal model
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

REGISTRY NUMBER: 93384-43-1 (botulinum toxin A)
9001-92-7 (endopeptidase)

L86 ANSWER 22 OF 26 TOXCENTER COPYRIGHT 2004 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2000:104043 TOXCENTER
COPYRIGHT: Copyright 2004 ACS
DOCUMENT NUMBER: CA13213161319V
TITLE: Role of neurotrophins and **lectins** in prevention of ototoxicity
AUTHOR(S): Gao, Wei-Qiang
CORPORATE SOURCE: Department of Neuroscience, Genentech, Inc., South San Francisco, CA, 94080, USA.
SOURCE: Annals of the New York Academy of Sciences, (1999) Vol. 884, No. Ototoxicity, pp. 312-327.
CODEN: ANYAA9. ISSN: 0077-8923.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2000:14944
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20020409

ABSTRACT:
A review with 48 refs. Degeneration of hair cells (HC) and/or spiral ganglion ***neurons*** (SGN) is a major cause of hearing loss. Postnatal rat cochlear explant cultures are used to study the toxic actions of different classes of ototoxins and to identify mols. that can protect SGN and HC from ototoxic damage. Various ototoxins induce differential damage to HC and/or SGN. While gentamicin preferentially causes HC death, sodium salicylate selectively induces degeneration of SGN. In contrast, cisplatin results in destruction of

both SGN and HC. Specific neurotrophins, including NT-4/5, BDNF, and NT-3, greatly protect SGN from all three types of ototoxins. In contrast, NGF and other growth factors have no effect. Of the 51 compds. examd., only Con A, a ***lectin*** mol., significantly protects HC from gentamicin. A dose-dependent study of Con A shows that maximal protection occurred at 100 nM. Further expts. indicates that preincubation of Con A with gentamicin does not form a complex, and coaddn. of Con A and gentamicin to bacterial cultures, such as E. Coli cultures, does not interfere with the antibiotic activity of gentamicin. When the other 21 **lectins** are examd., **Erythrina** ***cristagalli*** **lectin** and Detura stramonium **lectin** also show activity similar to Con A. These findings may help elucidate the mechanisms of ototoxins and suggest that specific neurotrophins and ***lectins*** may be of therapeutic value in the prevention of ototoxin-induced hearing loss.

CLASSIFICATION CODE: 2-0

SUPPLEMENTARY TERMS: Miscellaneous Descriptors
review neurotrophin **lectin** hearing loss
inhibition ear

L86 ANSWER 23 OF 26 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-611684 [58] WPIDS
DOC. NO. CPI: C2000-183090
TITLE: Manufacturing a medicament for modulating **C-fiber neurone** activity and treating e.g. pain, psoriasis, inflammation or mucus hypersecretion, comprises using a **lectin** or a nucleic acid encoding a **lectin**.
DERWENT CLASS: B04 D16
INVENTOR(S): CHADDOCK, J A; FOSTER, K A; QUINN, C P
PATENT ASSIGNEE(S): (MICR-N) MICROBIOLOGICAL RES AUTHORITY
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2000057897	A1	20001005	(200058)*	EN	62	A61K038-16
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW						
AU 2000035690	A	20001016	(200106)			A61K038-16
EP 1165114	A1	20020102	(200209)	EN		A61K038-16
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI						
JP 2002540162	W	20021126	(200307)		55	A61K038-00

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000057897	A1	WO 2000-GB1247	20000331
AU 2000035690	A	AU 2000-35690	20000331
EP 1165114	A1	EP 2000-914295	20000331
		WO 2000-GB1247	20000331
JP 2002540162	W	JP 2000-607647	20000331
		WO 2000-GB1247	20000331

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 2000035690	A	Based on	WO 2000057897
EP 1165114	A1	Based on	WO 2000057897
JP 2002540162	W	Based on	WO 2000057897

PRIORITY APPLN. INFO: GB 1999-7429 19990331

INT. PATENT CLASSIF.:

MAIN: A61K038-00; A61K038-16

SECONDARY: A61K047-48; A61K048-00; A61P001-06; A61P011-02; A61P011-06; A61P017-00; A61P017-06; A61P019-02; A61P025-00; A61P025-04; A61P025-06; A61P029-00; A61P043-00; C07K014-42; C07K019-00; C12N015-09; C12N015-29; C12P021-02

BASIC ABSTRACT:

WO 200057897 A UPAB: 20001114

NOVELTY - Manufacturing (M1) a medicament for modulation of **C-fiber neurone** activity using a **lectin**.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) manufacturing (M2) a medicament for modulation of **C-fiber neurone** activity using a nucleic acid that encodes a **lectin**;

(2) a pharmaceutical composition comprising a **lectin**, where the composition is free of Clostridial neurotoxin enzyme activity;

(3) a composition comprising one or more nucleic acid sequences encoding **lectins**;

(4) a conjugate comprising a **lectin** coupled to a peptide or protein that is free of Clostridial neurotoxin enzyme activity and optionally has a **C-fiber** modulation activity;

(5) a nucleic acid encoding (4);

(6) manufacturing (M3) a medicament for modulation of **C-fiber** activity, using (2), (3), (4), or (5);

(7) treating pain, psoriasis, inflammation or mucus hypersecretion using a medicament manufactured with a **lectin** or a nucleic acid encoding a **lectin**;

(8) inhibiting **C-fiber** activity using a composition of (M1), (M2), or (M3);

(9) stimulating **C-fiber** activity using a composition of (M1), (M2), or (M3);

(10) modulating **C-fiber** activity comprising administering a **lectin**, (2), (3), (4) or (5) to a patient;

(11) preparing (4) comprising coupling together, optionally via a linker, a **lectin** and a peptide or protein; and

(12) preparing (4) comprising expressing (5) in a hart, optionally including a linker nucleic acid sequence located within (5) to provide a linker molecule between the **lectin** and the peptide or protein of the conjugate.

ACTIVITY - Analgesic; antipsoriatic; antiinflammatory; mucolytic; antiasthmatic; antiulcer; antiarthritic; antiallergic; antimigraine. The analgesic effects of a galactosyl-reactive **lectin** IB4 from Bandeiraea simplicifolia were studied in vivo, in adult outbred mice (MF1) of either sex,with a weight range of 10 - 30 g. The mice were anaesthetized and a 5 mm incision was made in the skin above the spinal column. **Lectin** IB4 was injected in a single dose into an intrathecal space. The incision was closed using a single wound clip and the mice became fully mobile within two minutes. The effect over a 10 hour period was monitored. A significant increase in withdrawal latency was observed at 1 hour post application with an apparent maximal activity at 4 hours (15.0 and 17.6 seconds, respectively, compared to 11.6 and 12.4 seconds for a control group injected with phosphate buffered saline (PBS)). Analgesia was still clearly discernable over control-group animals at 10 hours post application (15.7 seconds for IB4 injected

animals and 12.7 seconds for PBS-injected animals).

MECHANISM OF ACTION - Substance P release modulator; **C-fiber** activity modulator. Embryonic dorsal rot ganglia (eDRG) were prepared from rats. An **Erythrina cristagalli lectin**-protein conjugate was applied to the eDRG and the substance P released was assayed. The percent inhibition of release was about 5 % at a concentration of 0.1 micro g/ml and was -45 % at 10 micro g/ml of the conjugate, demonstrating that the conjugate modulated release of substance P from an in vitro model of **C-fibers**.

USE - The new method is used for manufacturing a medicament for modulating **C-fiber neurone** activity, using a **lectin** or nucleic acid encoding a **lectin** (claimed). The medicament can be used to treat pain, psoriasis, inflammation or mucus hypersecretion (claimed). It can also be used to treat asthma, ulcer formation, headache, migraine, arthritis, and irritable bowel syndrome.

Dwg.0/14

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: B04-E03F; B04-L01; B04-N04; B12-M01A; B12-M02; B14-C01; B14-C03; B14-C09; B14-E08; B14-E10C; B14-G02A; B14-K01A; B14-K01E; B14-N16; B14-N17C; D05-H17C

L86 ANSWER 24 OF 26 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2003:682796 SCISEARCH
THE GENUINE ARTICLE: 707JA
TITLE: Isolation of the gene and large-scale expression and purification of recombinant **Erythrina cristagalli lectin**
AUTHOR: Stancombe P R (Reprint); Alexander F C G; Ling R; Matheson M A; Shone C C; Chaddock J A
CORPORATE SOURCE: Ctr Appl Microbiol & Res, Salisbury SP4 0JG, Wilts, England (Reprint)
COUNTRY OF AUTHOR: England
SOURCE: PROTEIN EXPRESSION AND PURIFICATION, (AUG 2003) Vol. 30, No. 2, pp. 283-292.
Publisher: ACADEMIC PRESS INC ELSEVIER SCIENCE, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA.
ISSN: 1046-5928.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 15
ABSTRACT:

Using polymerase chain reaction, the coding sequence for **Erythrina** ***cristagalli*** **lectin** (ECL) has been cloned and expressed in Escherichia coli. The amplified DNA sequence of ECL is highly homologous to that previously reported for **Erythrina** corallodendron **lectin** (ECorL), confirming the absence of introns in the ECL gene. The polypeptide sequences of ECL and ECorL have been compared and five amino acids have been identified that differentiate the two proteins. Recombinant E. ***cristagalli*** **lectin** (recECL) was expressed in E. coli from a genomic clone encoding the mature E. **cristagalli lectin** gene. Constitutive expression localised recombinant protein in inclusion bodies, which were solubilised, and recECL, subsequently refolded and purified by lactose affinity chromatography. Significant advantages were observed for purification from inclusion bodies rather than from a clone optimised to express soluble protein. A large-scale purification scheme has been developed that can prepare functional recECL from inclusion bodies with a yield of 870 mg/L culture. By the range of characterisation methods employed in this study, it has been demonstrated that recECL is functionally equivalent to native ECL obtained from the E. **cristagalli** plant. In addition, characterisation of the binding of radiolabelled recECL to cultured dorsal root ganglia

demonstrated that recECL binds to a single pool of receptors. (C) 2003 Elsevier Science (USA). All rights reserved.

CATEGORY: BIOCHEMICAL RESEARCH METHODS; BIOCHEMISTRY & MOLECULAR BIOLOGY; BIOTECHNOLOGY & APPLIED MICROBIOLOGY

SUPPLEMENTARY TERM: **Erythrina cristagalli**; **Erythrina**-related **lectins**; cloning; bacterial expression system; lactose affinity

SUPPL. TERM PLUS: DORSAL-ROOT GANGLIA; ESCHERICHIA-COLI; CORALLODENDRON **LECTIN**; AGGLUTININ; PROTEINS; CLONING; SITE; RAT; RECOGNITION; **NEURONS**

REFERENCE(S):

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)
ADAR R	1997	249	684	EUR J BIOCHEM
ARANGO R	1992	205	575	EUR J BIOCHEM
ARANGO R	1990	264	109	FEBS LETT
CHAO Q M	1994	313	346	ARCH BIOCHEM BIOPHYS
DUGGAN M J	2002	277	34846	J BIOL CHEM
LONGSTAFF M	1998	252	59	EUR J BIOCHEM
MORENO E	1997	36	4429	BIOCHEMISTRY-US
POLYAK S W	1997	10	615	PROTEIN ENG
SHARMA V	1996	389	289	FEBS LETT
SHARON N	1990	4	3198	FASEB J
SHARMA V	1994	148	299	GENE
SHARON N	1995	30	59	ESSAYS BIOCHEM
STREIT W J	1985	33	1042	J HISTOCHEM CYTOCHEM
SVENSSON C	2002	321	69	J MOL BIOL
WELCH M J	2000	38	245	TOXICON

L86 ANSWER 25 OF 26 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

ACCESSION NUMBER: 92:195554 SCISEARCH

THE GENUINE ARTICLE: HK198

TITLE: BANDEIRAEA-SIMPLICIFOLIA **LECTIN**-I AND VICIA-VILLOSA AGGLUTININ BIND SPECIFICALLY TO THE VOMERONASAL AXONS IN THE ACCESSORY OLFACTORY-BULB OF THE RAT

AUTHOR: ICHIKAWA M (Reprint); OSADA T; IKAI A

CORPORATE SOURCE: TOKYO METROPOLITAN INST NEUROSCI, DEPT ANAT & EMBRYOL, 2-6 MUSASHIDAI, FUCHU, FUCHU, TOKYO 183, JAPAN (Reprint); TOKYO INST TECHNOL, FAC BIOSCI & BIOTECHNOL, DEPT BIOL SCI, YOKOHAMA, KANAGAWA 227, JAPAN

COUNTRY OF AUTHOR: JAPAN

SOURCE: NEUROSCIENCE RESEARCH, (FEB 1992) Vol. 13, No. 1, pp. 73-79.
ISSN: 0168-0102.

DOCUMENT TYPE: Note; Journal

FILE SEGMENT: LIFE

LANGUAGE: ENGLISH

REFERENCE COUNT: 14

ABSTRACT:

The binding of 21 **lectins** to the accessory olfactory bulb (AOB) of the rat was examined by histochemistry. Two **lectins** [Bandeiraea simplicifolia **lectin** I (BSL-I) and Vicia villosa agglutinin (VVA)] bound specifically to the vomeronasal (VN) axons in the AOB. Seven ***lectins*** (Datura stramonium **lectin**, **Erythrina** ***cristagalli*** **lectin**, Lycoperisicon esculentum **lectin** , Ricinus communis agglutinin I, soybean agglutinin, Solanum tuberosum ***lectin*** , and Ulex europaeus agglutinin) bound to both VN axons in AOB and olfactory axons in the main olfactory bulb. BSL-I and VVA are useful as the marker of VN axons. This selective binding of **lectins** indicates

Not C-fibre

the presence of specific glycoconjugates on the surface of VN axons.

CATEGORY: NEUROSCIENCES
SUPPLEMENTARY TERM: **LECTIN**; GLYCOCONJUGATES; VOMERONASAL SYSTEM; ACCESSORY OLFACTORY BULB; RAT
SUPPL. TERM PLUS: MEDIAL AMYGDALOID NUCLEUS; ADULT-RAT; SYNAPTIC REORGANIZATION; NERVOUS-SYSTEM; FIBERS; RECOVERY; **NEURONS**; LESION; RABBIT
RESEARCH FRONT: 91-0209 002; VOMERONASAL ORGAN; RAT OLFACTORY EPITHELIUM; MALE HAMSTERS; SEXUAL PHEROMONES

REFERENCE(S):

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)
BARBER P C	1989	30	1	NEUROSCIENCE
HALPERN M	1987	10	325	ANNU REV NEUROSCI
ICHIKAWA M	1987	420	243	BRAIN RES
ICHIKAWA M	1987	420	253	BRAIN RES
ICHIKAWA M	1988	451	248	BRAIN RES
ICHIKAWA M	1989	498	45	BRAIN RES
IMAMURA K	1985	328	362	BRAIN RES
KEY B	1986	69	131	NEUROSCI LETT
MORI K	1986	365	404	BRAIN RES
MORI K	1987	408	215	BRAIN RES
MORI K	1987	20	259	NEUROSCIENCE
SCHWARTING G A	1991	547	239	BRAIN RES
STREIT W J	1985	33	1042	J HISTOCHEM CYTOCHEM
WYSOCKI C J	1979	3	301	NEUROSCIENCE BIOBEHA

L86 ANSWER 26 OF 26 USPATFULL on STN
ACCESSION NUMBER: 2002:314377 USPATFULL
TITLE: Endomural therapy
INVENTOR(S): Slepian, Marvin J., Tucson, AZ, UNITED STATES
PATENT ASSIGNEE(S): Endoluminal Therapeutics, Inc. (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002176849	A1	20021128
APPLICATION INFO.:	US 2002-72766	A1	20020208 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-267578P	20010209 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Patrea L. Pabst, Holland & Knight LLP, One Atlantic Center, Suite 2000, 1201 West Peachtree Street, Atlanta, GA, 30309-3400
NUMBER OF CLAIMS: 33
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Page(s)
LINE COUNT: 1277
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods, devices and materials for the treatment or repair, replacement, transplantation or augmentation of tissues in endomural zones specifically by open surgical, minimally invasive or percutaneous transmural or trans parenchymal application of polymeric material alone or in combination with bioactive agents or cells, have been developed. These methods and systems are useful to repair, alter function, replace

function or augment function of the central or endomural aspects of solid organs or tubular body structures.

PI US 2002176849 A1 20021128

DETD [0082] Polymers with free carboxylic acid or other anionic groups (e.g., sulfonic acid), such as the acrylic acid polymers noted above, can be used alone or added to other polymeric formulations to enhance tissue adhesiveness. Alternatively, materials that have tissue binding properties can be added to or bound to the polymeric material. Peptides with tissue adhesion properties are discussed below. Lectins that can be covalently attached to a polymeric material to render it target specific to the mucin and mucosal cell layer could be used. Useful lectin ligands include lectins isolated from: Abrus precatroius, Agaricus bisporus, Anguilla anguilla, Arachis hypogaea, Pandeiraea simplicifolia, Bauhinia purpurea, Caragan arobreseens, Cicer arietinum, Codium fragile, Datura stramonium, Dolichos biflorus, **Erythrina** corallodendron, **Erythrina** cristagalli, Euonymus europaeus, Glycine max, Helix aspersa, Helix pomatia, Lathyrus odoratus, Lens culinaris, Limulus polyphemus, Lysopersicon esculentum, Maclura pomifera, Momordica charantia, Mycoplasma gallisepticum, Naja mocambique, as well as the lectins Concanavalin A, Succinyl-Concanavalin A, Triticum vulgaris, Ulex europaeus I, II and III, Sambucus nigra, Maackia amurensis, Limax fluvus, Homarus americanus, Cancer antennarius, and Lotus tetragonolobus.

CLM What is claimed is:

31. The device of claim 15 for **nerve** regeneration.

IT **Nerve**

(cell or stem cell; endomural therapy)

IT 9001-92-7, Protease 9061-61-4, **Nerve** growth factor 62031-54-3, Fibroblast growth factor 62229-50-9, Epidermal growth factor 81669-70-7, Metalloprotease

(endomural therapy)

FILE 'HOME' ENTERED AT 12:59:43 ON 03 JUN 2004